The American Journal of

CARDIOLOGY

OFFICIAL JOURNAL OF THE American College of Cardiology

Symposium on Cardiology in Aviation

LAWRENCE E. LAMB, M.D.
Guest Editor

A PUBLICATION OF THE Yorke GROUP

JULY 1960

Your angina patient hardly knows where one leaves off and the other begins. What he does recognize is the relief he gets from both when you prescribe CARTRAX.

FOR ANGINAL PAIN

PETN (pentaerythritol tetranitrate) is "... the most effective drug currently available for prolonged prophylactic treatment of angina pectoris."[1]

FOR CARDIAC PANIC

"I favor ATARAX [as the tranquilizer for the anxious cardiac] ... because there is an absence of side effects with this drug, and also because in cardiacs who are troubled with ectopic beats, ATARAX has a quinidine-like action."[2]

PETN + ATARAX®*

TOGETHER ONLY IN

CARTRAX®

Dosage: Begin with 1 to 2 yellow CARTRAX "10" tablets (10 mg. PETN plus 10 mg. ATARAX) 3 to 4 times daily. When indicated, this may be increased by switching to pink CARTRAX "20" tablets (20 mg. PETN plus 10 mg. ATARAX). For convenience, write "CARTRAX 10" or "CARTRAX 20." Supplied: In bottles of 100. Prescription only.

References: 1. Russek, H. I.: Postgrad. Med. 19:562 (June) 1956. 2. Russek, H. I.: Presented at the Symposium on the Management of Cardiovascular Problems of the Aged, Dade County Medical Association, Miami Beach, April 12, 1958.

*brand of hydroxyzine

ROERIG Rx

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being™

WHY *ALDACTONE*®
IN EDEMA

Because it acts by regulating a basic physiologic imbalance, Aldactone possesses multiple therapeutic advantages in treating edema.

Aldactone inactivates a crucial mechanism producing and maintaining edema — the effect of excessive activity of the potent salt-retaining hormone, aldosterone. This corrective action produces a satisfactory relief of edema even in conditions wholly or partially refractory to other drugs.

Also, Aldactone acts in a different manner and at a different site in the renal tubules than other drugs. This difference in action permits a true synergism with mercurial and thiazide diuretics, supplementing and potentiating their beneficial effects.

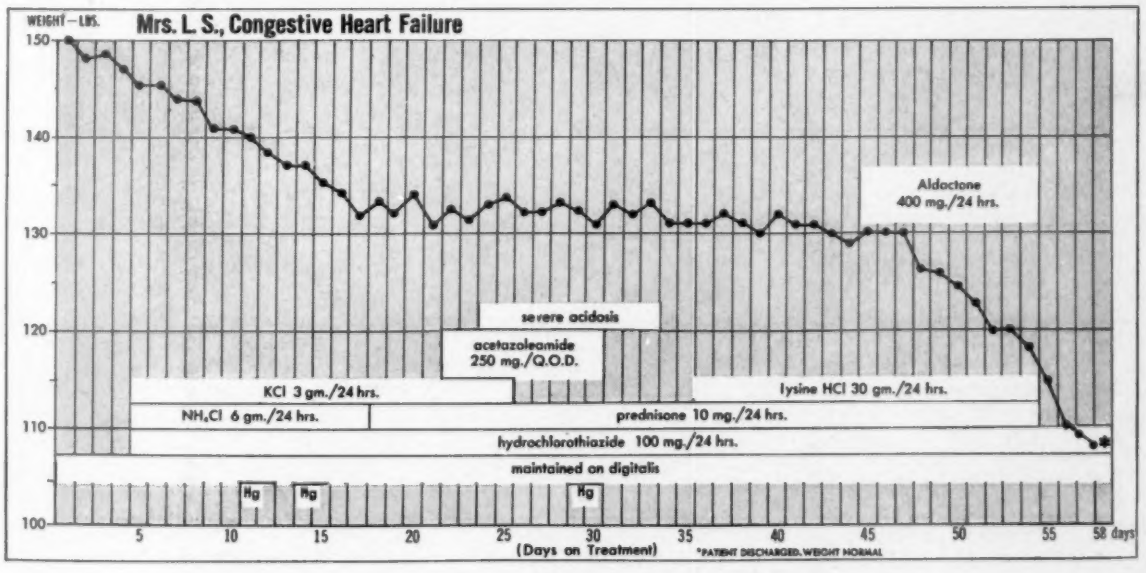
Further, Aldactone minimizes the electrolyte upheaval often caused by mercurial and thiazide compounds.

The accompanying graph shows a dramatic but by no means unusual instance of the effect of Aldactone in refractory edema.

The usual adult dosage of Aldactone, brand of spironolactone, is 400 mg. daily. Complete dosage information is contained in Searle New Product Brochure No. 52.

SUPPLIED: Aldactone is supplied as compression-coated yellow tablets of 100 mg.

G. D. SEARLE & CO., Chicago 80, Illinois.
Research in the Service of Medicine.



NOW...
A DRUG THAT LOWERS CHOLESTEROL LEVELS AS MUCH AS 200 mg.%
WITH VIRTUALLY NO ANNOYING SIDE EFFECTS
...AND NO DIETARY RESTRICTIONS

NICALEX*

TABLETS aluminum nicotinate, Walker

New NICALEX reduces blood cholesterol levels as much as 200 mg. % with no flushing, itching or gastrointestinal disturbance in over 80% of patients.[1-5] Significant reductions have been obtained in close to 90% of hypercholesteremic patients to date.[1-5] Lowered cholesterol levels can be maintained indefinitely with little or no discomfort to the patient. And there is no need to restrict the diet throughout therapy.

A newly synthesized salt of nicotinic acid, NICALEX is "...as effective in reducing blood cholesterol as plain nicotinic acid...."[5] But unlike the older therapy, which produces vasomotor and gastrointestinal side effects in the vast majority of patients, NICALEX is characterized by a markedly reduced incidence of unpleasant reactions.[5]

NICALEX is so well tolerated because it is hydrolyzed *slowly* and *uniformly* in the gastrointestinal tract into aluminum hydroxide, an effective buffering agent, plus active nicotinic acid. Thus, a sustained cholesterol-lowering action can be readily maintained with virtually no unwanted effects.

Dosage: 2 to 4 tablets t.i.d., with or after meals. Each tablet contains aluminum nicotinate (Walker) equivalent in biological activity to 500 mg. of nicotinic acid.

Supplied: Bottles of 100 and 1000.

References: **1.** Tandowsky, R. M.: Personal communication. **2.** Parsons, W. B.: *Curr. Therapeut. Res.* 2:137 (May) 1960. **3.** Thompson, C. E.: Personal communication. **4.** Biben, L. H.; Kurstin, W., and Protas, M.: Personal communication. **5.** Hobbs, T. G.: Personal communication.

*PAT. PENDING

Walker LABORATORIES, INC., MOUNT VERNON, N. Y.

Symbol of Distinguished Journalism

The American Journal of Cardiology

THE AMERICAN JOURNAL OF CARDIOLOGY is published monthly by The American Journal of Medicine, Inc., Executive and Editorial Offices, 11 East 36th Street, New York 16, N. Y. July 1960, Volume 6, No. 1. Publication Office, 20th and Northampton Streets, Easton, Pa. Second-class postage paid at Easton, Pa. Official Journal of the American College of Cardiology.

SUBSCRIPTIONS: United States $12.00 a year; Canada $13.00; Foreign $15.00
SINGLE COPIES: Regular Issues $2.00; Symposium and Special Issues $4.00

MAIL CHANGES OF ADDRESS AND SUBSCRIPTION ORDERS TO: The American Journal of Cardiology, 11 East 36th Street, New York 16, N. Y. Change of address must reach us one month in advance.

MANUSCRIPTS: All manuscripts should be typewritten double space and submitted in duplicate to the Editorial Office of The American Journal of Cardiology, 11 East 36th Street, New York 16, N. Y. The top should be indicated on the back of each photograph. Reference style: Smith, J. S. Treatment of cardiac failure. *Am. J. Cardiol.*, 3: 274, 1959.

AMERICAN COLLEGE OF CARDIOLOGY: All communications for the College should be addressed to the American College of Cardiology, Office of the Executive Director, 350 Fifth Ave., New York 1, N. Y.

PLINY A. PORTER—Publisher
JOHN J. MARTIN—Assistant Publisher

The American Journal of Cardiology

Volume VI JULY 1960 Number 1

CONTENTS

Symposium on Cardiology in Aviation

Contents continued on page 7

CONTENTS continued—July 1960

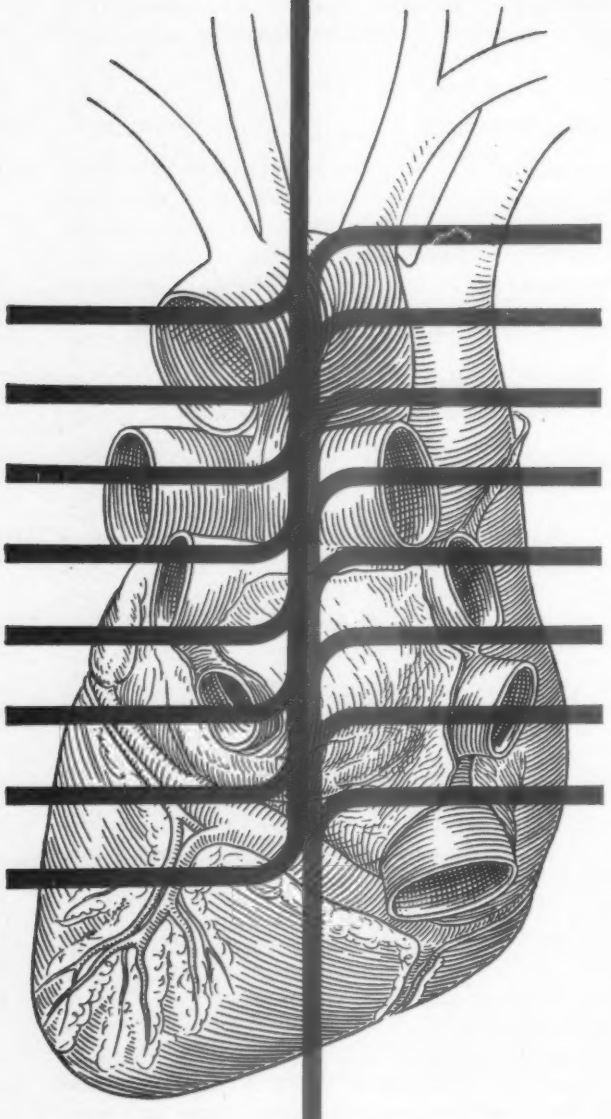
VOLUME SIX NUMBER ONE

Contents continued on page 9

new approach to the concept of "total management" in angina pectoris

new Marplan

a happy balance of potency/safety



Marplan prevents or reduces anginal pain: Marplan is indicated primarily for patients with moderately severe to intractable angina pectoris. It has demonstrated a high degree of effectiveness. When used on a continuous dosage schedule, Marplan prevents pain, increases exercise tolerance and reduces nitroglycerin requirements.

Marplan creates a more confident mental climate: Many angina patients display a more cheerful outlook when on Marplan therapy. This mental improvement is undoubtedly due to the antidepressive action of Marplan. However, it should be stressed that Marplan is indicated for *symptomatic* control of angina pectoris. While it abolishes anginal pain (some patients may achieve a virtually pain-free state), Marplan does not appear to influence the EKG. Hence, as with previously available prophylactic agents, it is imperative that patients be instructed to maintain the same restriction of activity in force prior to Marplan therapy.

Marplan strikes a happy balance of potency/safety: Marplan has been shown to be considerably more potent than certain other amine oxidase regulators. While clinically such increase in potency may be associated with increased side effects, Marplan strikes a happy balance of potency/safety. Marplan has shown markedly fewer of certain of the side reactions of the hydrazines and, moreover, in thousands of cases, there have been no reports of hepatitis attributable to Marplan. Nevertheless, all precautions set forth in the product literature should be strictly observed. Since the precise manner in which Marplan improves the cardiac status is as yet undefined, and since so many patients attain a virtually pain-free state, it is imperative that patients be instructed to maintain the same restrictions of activity in force prior to Marplan therapy.

Complete dosage information, available on request, should be consulted before prescribing Marplan.

MARPLAN™—brand of isocarboxazid

ROCHE
LABORATORIES
Division of
Hoffmann-La Roche Inc.
Nutley 10, N.J.

CONTENTS continued—July 1960

VOLUME SIX NUMBER ONE

Contents continued on page 11

VISTARIL®

hydroxyzine pamoate

relieves associated anxiety in the cardiac patient

IN BRIEF

VISTARIL gently calms the fears of the cardiac patient. It permits the patient to remain calm but alert, because it is not a cortical depressant. An ideal adjunct in the treatment of heart disease, it may be used concurrently with digitalis or other medications.

INDICATIONS: VISTARIL is a rapid-acting tranquilizer with a wide margin of safety. It is effective in the symptomatic treatment of a variety of neuroses and other emotional disturbances manifested by anxiety, apprehension or fear — whether occurring alone or complicating a physical illness.

ADMINISTRATION & DOSAGE: VISTARIL dosage varies with individual requirements and ranges from 25 mg. t.i.d. to 100 mg. q.i.d. for adults. The usual dosage for children *under* 6 years is 50 mg. daily in divided doses; children *over* 6 years — 50 to 100 mg. in divided doses. For parenteral dosage information consult package insert.

SIDE EFFECTS: Drowsiness may occur in some patients; if so, it is usually transitory, disappearing within a few days of continued therapy or upon reduction of dosage. Dryness of mouth may be encountered at higher doses.

PRECAUTIONS: The potentiating action of hydroxyzine is mild, but must be taken into consideration when the drug is used in conjunction with central nervous system depressants.

SUPPLY: *Capsules* — 25, 50, and 100 mg. *Oral Suspension* — 25 mg. per 5 cc. teaspoonful. *Parenteral Solution* (as the HCl) — 10 cc. vials and 2 cc. Steraject® Cartridges, 25 mg. per cc.; 2 cc. ampules, 50 mg. per cc.

Detailed professional information is available on request from Pfizer Laboratories Medical Department.

Science for the world's well-being™

Pfizer

PFIZER LABORATORIES
Div., Chas. Pfizer & Co., Inc.
Brooklyn 6, N. Y.

CONTENTS continued—July 1960

VOLUME SIX NUMBER ONE

Index to Advertisers on page 48

Proven

in over five years of clinical use
and more than
750 published clinical studies

Effective

FOR RELIEF OF ANXIETY
AND TENSION

Outstandingly Safe

Miltown®

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets;
or as MEPROTABS*—400 mg. *unmarked*, coated tablets.

*Trade-mark

1 simple dosage schedule produces rapid, reliable tranquilization without unpredictable excitation

2 no cumulative effects, thus no need for difficult dosage readjustments

3 does not produce ataxia, change in appetite or libido

4 does not produce depression, Parkinson-like symptoms, jaundice or agranulocytosis

5 does not impair mental efficiency or normal behavior

Miltown®
meprobamate (Wallace)

WALLACE LABORATORIES / *New Brunswick, N. J.*

PUBLISHER'S INFORMATION PAGE

The Editors and Publishers of THE AMERICAN JOURNAL OF CARDIOLOGY welcome concise articles on new findings in cardiology. As is customary in professional publications, statements in articles are the responsibility of the authors; articles must be contributed solely to THE AMERICAN JOURNAL OF CARDIOLOGY; material is copyrighted and may not be reproduced without permission of the publishers.

Preparation of Manuscripts

Authors are requested to follow these instructions carefully in preparing manuscripts: Please double space with good margins; type on one side of the sheet only; make a carbon copy for yourself and send the original with one carbon copy to the editor; include staff position and connection; list bibliographic references in chronological order as referred to in text at the end of the article (not in footnotes). Please make certain each reference contains the name of author with initials; title of article; name of periodical, with volume, page and year. For example: Smith, J. S. Treatment of cardiac failure. Am. J. Card., 3:274, 1959.

Preparation of Illustrations

So that your article will be presented most effectively, illustrations must be glossy prints or professional drawings in black ink (never in blue; it will not reproduce well). Reference to all illustrations should be inserted in the text in consecutive order. Please follow these identification instructions: Write the figure number and the author's name on the back of each illustration and indicate the top.

Type legends for illustrations on a separate sheet with numbers corresponding to those on the photographs or drawings. Please do not attach legends to the pictures.

A reasonable number of illustrations are supplied free of cost; we know the authors will understand that special arrangements must be made with the publishers for excess illustrations and tables.

Reviews, Abstracts

Books for review may be sent directly to the Editor, Simon Dack, M.D., The American Journal of Cardiology, 11 E. 36th St., New York 16.

Permission to abstract must be obtained from the publisher. Only paid circulation journals will be permitted to abstract.

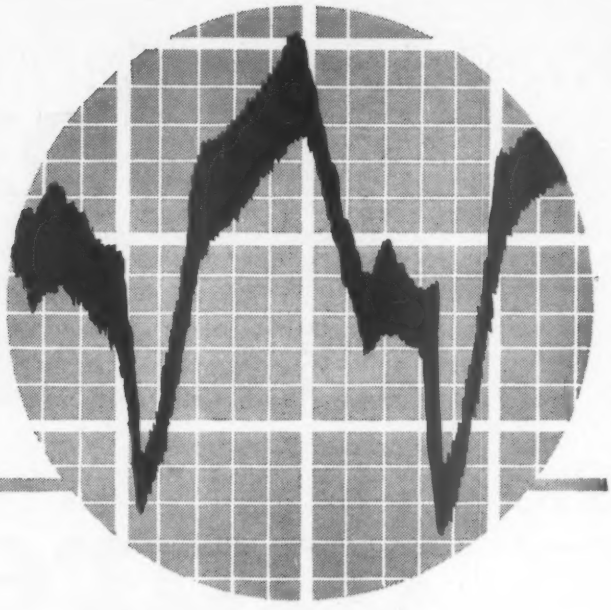
Reprints

Orders for reprints of articles should be sent directly to the Publisher, The American Journal of Cardiology, 11 East 36th Street, New York 16, N. Y. Prices are quoted after articles are published.

The American Journal of Cardiology

11 East 36th Street, New York 16, New York

prompt
treatment
of cardiac
arrhythmias



injectable

QUINIDINE

hydrochloride

Injectable Quinidine Hydrochloride, Brewer—the first injectable quinidine available in America—is especially indicated in ventricular tachycardia and in certain cases of auricular fibrillation. It usually begins to act within 15 to 30 minutes, and reaches its maximum effect in 1½ to 3 hours. In one study of 107 cases of paroxysmal ventricular tachycardia, the investigators conclude: "The treatment of choice was quinidine therapy."[1] In refractory cases of paroxysmal tachycardia, the intravenous administration of Quinidine has proved effective.[2]

ADMINISTRATION: Intramuscularly, or if necessary, intravenously.

SUPPLIED: Quinidine Hydrochloride Injectable (0.6 gm.) in 5 cc. ampuls. Quinidine Hydrochloride Injectable (0.18 gm.) in 1½ cc. ampuls. Also available for oral administration—Quindul (Quinidine Sulfate, Brewer) (3 gr.) in capsules, tablets and enteric coated tablets.

Additional information and clinical reports forwarded on request

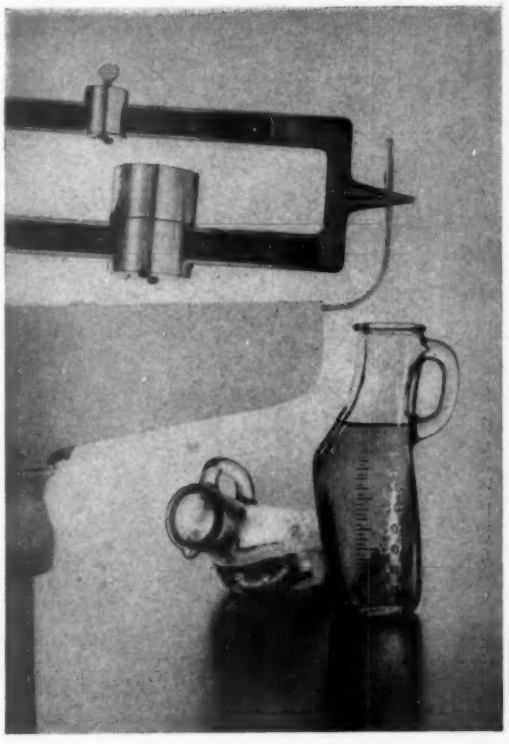
Brewer
Est. 1852

Brewer & Company, Inc.

WORCESTER 8 MASSACHUSETTS, U.S.A.

1. Armbrust, C.A., Jr., and Levine, S.A.: Paroxysmal Ventricular Tachycardia: A Study of 107 Cases. Circulation 1:28 (1950)
2. Bell, G.D., Bradley, R.B., and Hurxthal, L.M.: Paroxysmal Tachycardia, Experiences with Massive Doses of Quinidine Intravenously in a Refractory Case. Circulation 1:939 (1950)

6 important reasons why physicians choose Esidrix for *congestive heart failure, toxemia & edema of pregnancy, premenstrual edema, steroid-induced edema, edema of obesity*



1. Esidrix is one of the most effective oral diuretics known... 10 to 15 times more active than chlorothiazide.
2. Esidrix markedly increases sodium and chloride excretion, usually with minimal effect on excretion of potassium and bicarbonate.
3. Certain patients unresponsive to mercurials and chlorothiazide respond readily to Esidrix.
4. Esidrix alone can be used to reduce blood pressure. It also potentiates the action of such other antihypertensive agents as Singoserp, Serpasil, Apresoline, and ganglionic blockers.
5. Patients transferring from chlorothiazide to Esidrix frequently experience additional loss of retained body fluid and/or lower blood pressure levels.
6. In most cases, Esidrix permits moderation in severe sodium restriction, makes meals more palatable.

Esidrix®

(hydrochlorothiazide CIBA)

An improved analog of chlorothiazide, a product of CIBA research

SUPPLIED: Esidrix *Tablets*, 25 mg. (pink, scored) and 50 mg. (yellow, scored).

Complete information available on request.

CIBA
SUMMIT, NEW JERSEY

SINGOSERP® (syrosingopine CIBA)
SERPASIL® (reserpine CIBA)
APRESOLINE® hydrochloride (hydralazine hydrochloride CIBA) 2/2800MK

ONLY QUINAGLUTE® DURA-TAB S.M.® PROVIDES ORAL QUINIDINE GLUCONATE (5 gr.) ...BETTER TOLERATED

because it is 10 times as soluble as the sulfate

SAMPLES and literature—write...

REFER TO PDR Page 893

WYNN PHARMACAL CORPORATION

Lancaster Ave. at 51st St.
Philadelphia 31, Pa.

*U.S. Patent 2,895,881

in q. 12 h. dosage each Sustained Medication* dose maintains uniformly effective, virtually non-fluctuating blood levels, all day, all night.

in cardiac arrhythmias for maximum quinidine efficacy, tolerance, convenience[1-5]—specify Quinaglute Dura-Tab S.M. Bottles of 30, 100 and 250.

1. Bellet, S., Finkelstein, D., and Gilmore, H.: A.M.A. Archives Int. Med. 100:750, 1957. 2. Bellet, S.: Amer. Heart J. 56:479, 1958. 3. Bellet, S.: Amer. J. Cardiology 4:268, 1959. 4. Finkelstein, D.: Penn. Med. J. 61:1216, 1958. 5. DiPalma, J. R.: Progress in Cardiovascular Dis. 2:343, 1960.

also available: INJECTABLE QUINAGLUTE

a refinement in rauwolfia alkaloid therapy

moderil®

brand of rescinnamine

FOR BETTER MANAGEMENT OF HYPERTENSION

a purified alkaloid of rauwolfia . . . lessens the frequency and/or severity of these reserpine side effects:

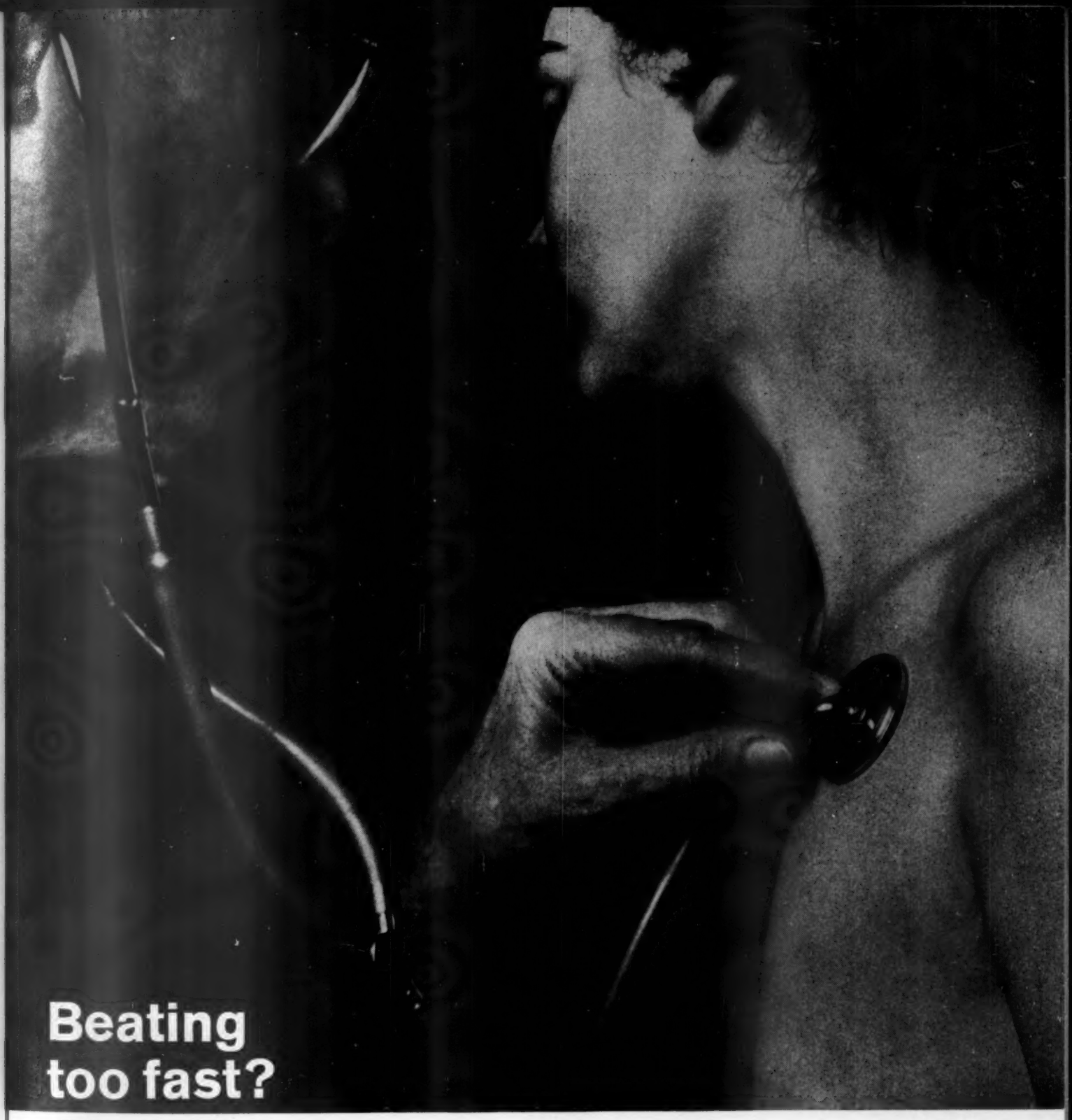
mental depression • bradycardia • sedation • weakness • fatigue • lassitude • sleepiness • nightmares • gastrointestinal effects

useful *alone* for gradual, sustained lowering of blood pressure in mild to moderate labile hypertension

useful *as an adjunct* to other types of antihypertensive agents, permitting their use in lower, better tolerated dosage

Professional information available on request

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc. Brooklyn 6, N.Y. Pfizer *Science for the world's well-being™*



Beating too fast?

Slow it down with SERPASIL®

(reserpine CIBA)

Serpasil has proved effective as a heart-slowing agent in the following conditions: mitral disease; myocardial infarction; cardiac arrhythmias; neurocirculatory asthenia; thyroid toxicosis; excitement and effort syndromes; cardiac neurosis; congestive failure. Serpasil should be used with caution in patients receiving digitalis and quinidine. It is not indicated in cases of aortic insufficiency.

SUPPLIED: Tablets, 0.1 mg., 0.25 mg. (scored) and 1 mg. (scored). Complete information available on request.

CIBA

SUMMIT • NEW JERSEY

S/2819MB

THE ANONYMOUS MYCOBACTERIA IN HUMAN DISEASE *edited by* **John S. Chapman,** *Univ. of Texas.* With contributions by 21 authorities whose skills and experience are outstanding. No other book exists in which can be found so comprehensive a review of all features of anonymous mycobacterial disease. Basic bacteriology of the anonymous mycobacteria is presented, placing them in their position with respect to other organisms, particularly the human tubercle organism. Experimental data is introduced to aid in an understanding of their location as pathogens. The book then summarizes and condenses all available information on pathology, epidemiology, clinical patterns, and therapeusis of human infections caused by these microorganisms. *Pub. date July '60*

THE CHEMISTRY OF LIPIDS IN HEALTH AND DISEASE: A review of our present knowledge of lipids, their chemical structure, their breakdown and synthesis in living organisms; their place in human nutrition; and their abnormalities of metabolism in disease *by* **H. K. King,** *Univ. of Liverpool.* A straightforward, clear summary which integrates the findings of workers over this wide and expanding field. Conveys the spirit of new ideas rather than becoming just a mere guide-book to literature or an attempt to revise older theories. *120 pp., 2 il.* (*Amer. Lec. Living Chemistry edited by I. Newton Kugelmass*), $3.75

ELECTRON MICROSCOPY OF THE CARDIOVASCULAR SYSTEM: An Electron Microscopic Study with Applications to Physiology *by* **Bruno Kisch,** *Yeshiva Univ.* PURPOSE: To acquaint the medical profession at large and particularly the cardiologist with the important contributions that electron microscopy has made to our understanding of the ultra microscopic structure and function of the cardiovascular system. The author's discovery of the function and vast quantity of enzyme bearing organisms (sacrosomes) within each muscle fiber of the heart opens new vistas for understanding the function of heart muscle. *Pub. date June '60*

THE SURGICAL TREATMENT OF PORTAL HYPERTENSION, BLEEDING ESOPHAGEAL VARICES AND ASCITES *by* **M. Judson Mackby,** *Kaiser Foundation Hospital, San Francisco.* To guide the surgeon through the confused tangle of conflicting theories and practices, Dr. Macky presents what is probably the first complete manual of practical clinical management of the surgical complications of cirrhosis—A COMPENDIUM OF ALL THAT IS KNOWN, SUSPECTED, OR INFERRED about this condition. Emphasis throughout on exact technique, including detailed descriptions of the various operative procedures currently in use. (*Amer. Lec. Surgery edited by Michael E. De Bakey and R. Glen Spurling*) *Pub. date Sept. '60*

7 NEW BOOKS FOR CARDIOLOGISTS

PAGES IN THE HISTORY OF CHEST SURGERY by Rudolf Nissen, *Univ. of Basel, Switzerland, and* **Roger H. L. Wilson,** *Univ. of Calif. School of Med., San Francisco.* The whole panorama of chest surgery unfolds—highlighting major developments for thoracic surgeons and delighting, we are sure, zealous students of medical history. Early figures and their attitudes not only on thoracic surgery but the ancillary sciences are brought to life. The change in attitude from surgery of pathologic anatomy to surgery of physiologic dysfunction unfolds. *Pub. date August '60*

THE CLINICAL USE OF ALDOSTERONE ANTAGONISTS *compiled and edited by* **Frederick C. Bartter.** Twenty-three experienced investigators survey the clinical and metabolic results of controlled clinical investigation with aldosterone antagonists in man. Coverage includes 1) The fundamental mechanism of action and clinical results with aldosterone antagonists used as a diagnostic tool 2) The use of aldosterone antagonists in patients with cirrhosis and ascites 3) Early experiences with aldosterone antagonists and patients with cardiac failure and edema and 4) Preliminary studies with the use of aldosterone antagonists in hypertension, nephrosis, and idiopathic edema. *Pub. June '60, 224 pp., 112 il., $5.00*

EMBOLIC DISPERSOIDS IN HEALTH AND DISEASE *by* **Gus Schreiber,** *Diplomate, American Board of Internal Med.* Based on four years of intensive investigation, this report demonstrates exogenous and endogenous embolic sized particles in significant numbers in the arterial and venous blood of human subjects. With PROFUSE SUBSTANTIATING EXHIBITS the many different types of embolic sized particles are classified. Their source, course in the body, and routes of elimination are demonstrated. *104 pp., 12 il.* (*Amer. Lec. Living Chemistry edited by I. Newton Kugelmass*), $5.50

CHARLES C THOMAS • PUBLISHER

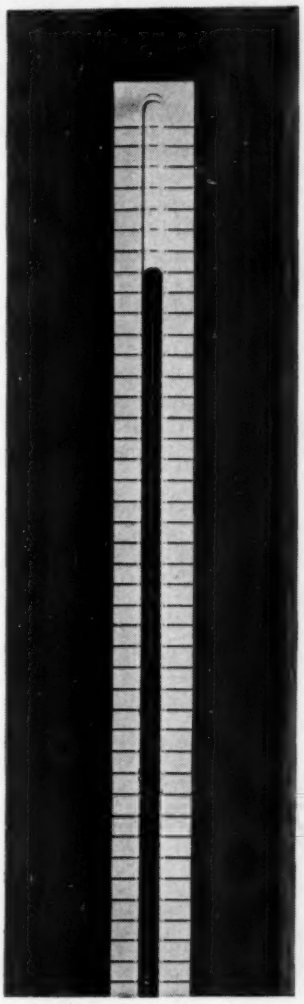
301-327 East Lawrence Avenue

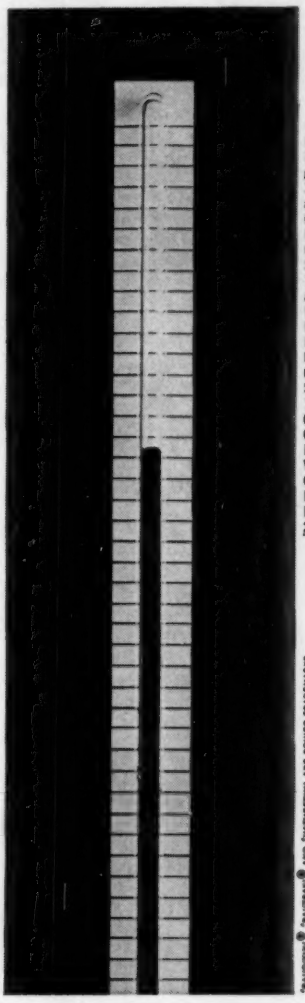
Springfield • Illinois

for a smooth downward curve

New Rautrax-N results in prompt lowering of blood pressure.[1] Rautrax-N, a new and carefully developed antihypertensive-diuretic preparation, provides improved therapeutic action[1] plus enhanced diuretic safety for all degrees of essential hypertension. A combination of Raudixin and Naturetin, Rautrax-N facilitates the management of hypertension when rauwolfia alone proves inadequate, or when prolonged treatment, with or without associated edema, is indicated.

Naturetin, the diuretic of choice, also possesses marked antihypertensive properties, thus complementing the known antihypertensive action of Raudixin. In this way a lower dose of each component in Rautrax-N controls hypertension effectively with few side effects and greater margin of safety.[1-16]





Other advantages are a balanced electrolyte pattern[1-16] and the maintenance of a favorable urinary sodium-potassium excretion ratio.[2-16] Clinical studies[1-5] have shown that the diuretic component of Rautrax-N—Naturetin—has only a slight effect on serum potassium. The supplemental potassium chloride provides additional protection against potassium depletion which may occur during long term therapy.

Rautrax-N may be used alone or in conjunction with other antihypertensive drugs, such as ganglionic blocking agents, veratrum or hydralazine, when such regimens are needed in the occasionally difficult patient.

Supply: Rautrax-N—capsule-shaped tablets providing 50 mg. Raudixin (Squibb Rauwolfia Serpentina Whole Root) and 4 mg. Naturetin (Squibb Benzydroflumethiazide), with 400 mg. potassium chloride.

Dosage: Initially-1 to 4 tablets daily after meals. Maintenance-1 or 2 tablets daily after meals; maintenance dosage may range from 1 to 4 tablets daily. For complete instructions and precautions see package insert. Literature available on request.

References: 1. Reports to the Squibb Institute, 1960. 2. David, N. A.; Porter, G. A., and Gray, R. H.: Monographs on Therapy 5:60 (Feb.) 1960. 3. Stenberg, E. S., Jr.; Benedetti, A., and Forsham, P. H.: Op. cit. 5:46 (Feb.) 1960. 4. Fuchs, M.; Moyer, J. H., and Newman, B. E.: Op. cit. 5:55 (Feb.) 1960. 5. Marriott, H. J. L., and Schamroth, L.: Op. cit. 5:14 (Feb.) 1960. 6. Ira, G. H., Jr.; Shaw, D. M., and Bogdonoff, M. D.: North Carolina M. J. 21:19 (Jan.) 1960. 7. Cohen, B. M.: M. Times, to be published. 8. Breneman, G. M. and Keyes, J. W.: Henry Ford Hosp. M. Bull. 7:281 (Dec.) 1959. 9. Forsham, P. H.: Squibb Clin. Res. Notes 2:5 (Dec.) 1959. 10. Larson, E.: Op. cit. 2:10 (Dec.) 1959. 11. Kirkendall, W. M.: Op. cit. 2:11 (Dec.) 1959. 12. Yu, P. N.: Op. cit. 2:12 (Dec.) 1959. 13. Weiss, S.; Weiss, J., and Weiss, B.: Op. cit. 2:13 (Dec.) 1959. 14. Moser, M.: Op. cit. 2:13 (Dec.) 1959. 15. Kahn, A., and Grenblatt, I. J.: Op. cit. 2:15 (Dec.) 1959. 16. Grollman, A.: Monographs on Therapy 5:1 (Feb.) 1960.

Squibb Quality—the Priceless Ingredient

SQUIBB

new

The proved, effective antihypertensive—now combined with a safer, better diuretic

RAUTRAX-N®

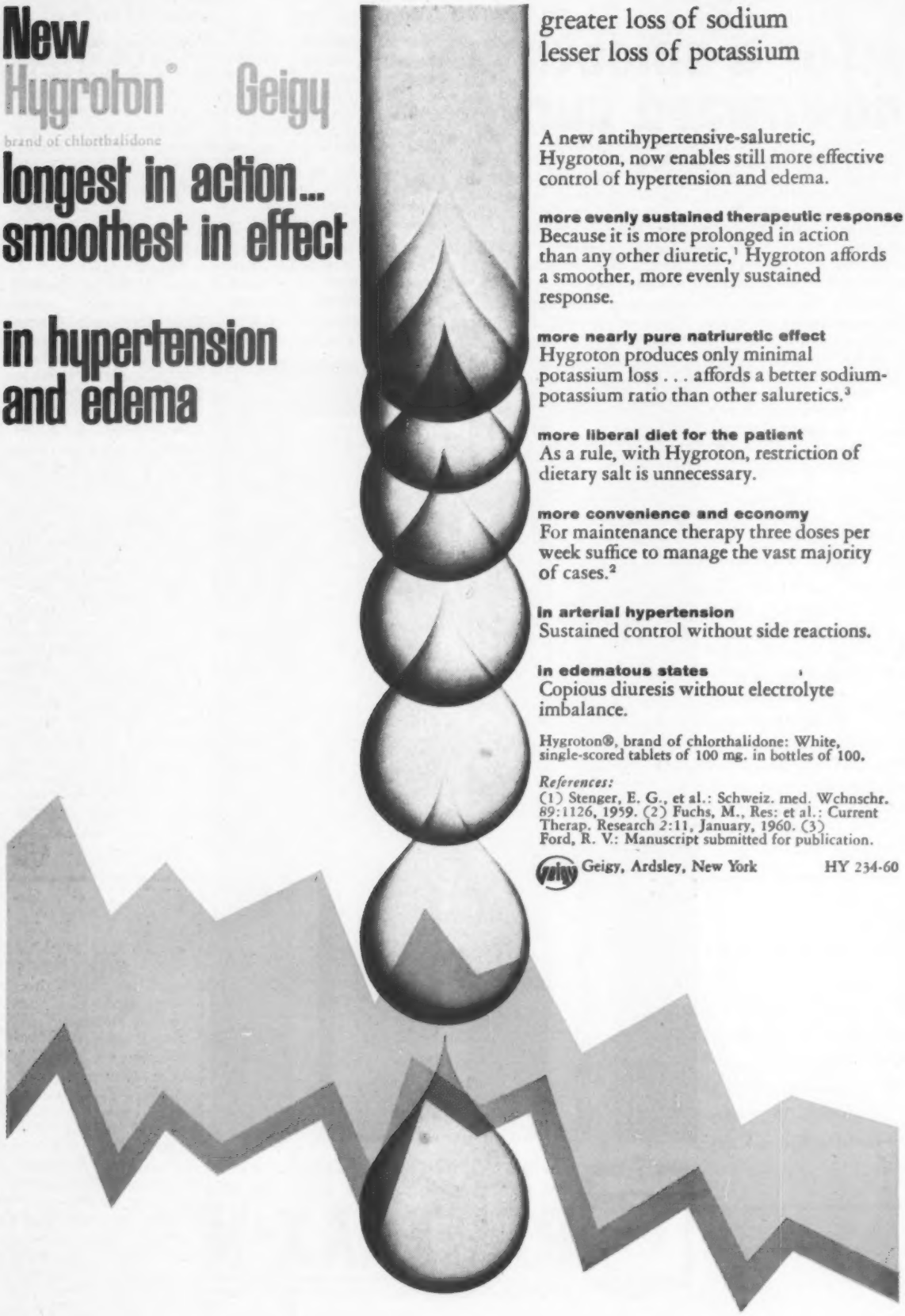
Squibb Standardized Whole Root Rauwolfia Serpentina (Raudixin) and Benzydroflumethiazide (®Naturetin) with Potassium Chloride

New Hygroton® Geigy

brand of chlorthalidone

longest in action... smoothest in effect

in hypertension and edema



greater loss of sodium
lesser loss of potassium

A new antihypertensive-saluretic, Hygroton, now enables still more effective control of hypertension and edema.

more evenly sustained therapeutic response
Because it is more prolonged in action than any other diuretic,[1] Hygroton affords a smoother, more evenly sustained response.

more nearly pure natriuretic effect
Hygroton produces only minimal potassium loss . . . affords a better sodium-potassium ratio than other saluretics.[3]

more liberal diet for the patient
As a rule, with Hygroton, restriction of dietary salt is unnecessary.

more convenience and economy
For maintenance therapy three doses per week suffice to manage the vast majority of cases.[2]

in arterial hypertension
Sustained control without side reactions.

in edematous states
Copious diuresis without electrolyte imbalance.

Hygroton®, brand of chlorthalidone: White, single-scored tablets of 100 mg. in bottles of 100.

References:
(1) Stenger, E. G., et al.: Schweiz. med. Wchnschr. 89:1126, 1959. (2) Fuchs, M., Res: et al.: Current Therap. Research 2:11, January, 1960. (3) Ford, R. V.: Manuscript submitted for publication.

Geigy, Ardsley, New York HY 234-60

new nitrate offers new benefits for anginal patients

Fremont[1] notes that ISORDIL ". . . has been very effective in increasing the exercise tolerance of patients and also reducing the number of attacks of angina pectoris of the decubital type." Prophylactically and therapeutically, ISORDIL provides four distinctive advantages.

rapid onset—ready solubility of ISORDIL produces benefits within 15 to 30 minutes (not intended to replace emergency use of nitroglycerin).

prolonged action—benefits of ISORDIL persist for at least 4 hours per oral dose of 10 mg.

consistent effect—85 per cent of patients[2] treated have responded favorably to ISORDIL. In comparative studies, Sherber[3] found ISORDIL better than other therapy in 17 of 18 patients.

unusual safety—only reported side reaction: transitory, easily-controlled headache.

Electrocardiographic studies by Russek[4] clearly show that ISORDIL produces a more favorable balance between oxygen supply and demand following the Master two-step test. He concludes that "ISORDIL is a new and effective agent for therapy of angina pectoris."

Literature and professional samples available on request.

1. Fremont, R.E.: Personal Communication (Dec., 1959).
2. Summary of Case Reports on File, Ives-Cameron Company.
3. Sherber, D.A.: Personal Communication (Oct., 1959).
4. Russek, H.I.: Personal Communication (Oct., 1959).

TABLETS

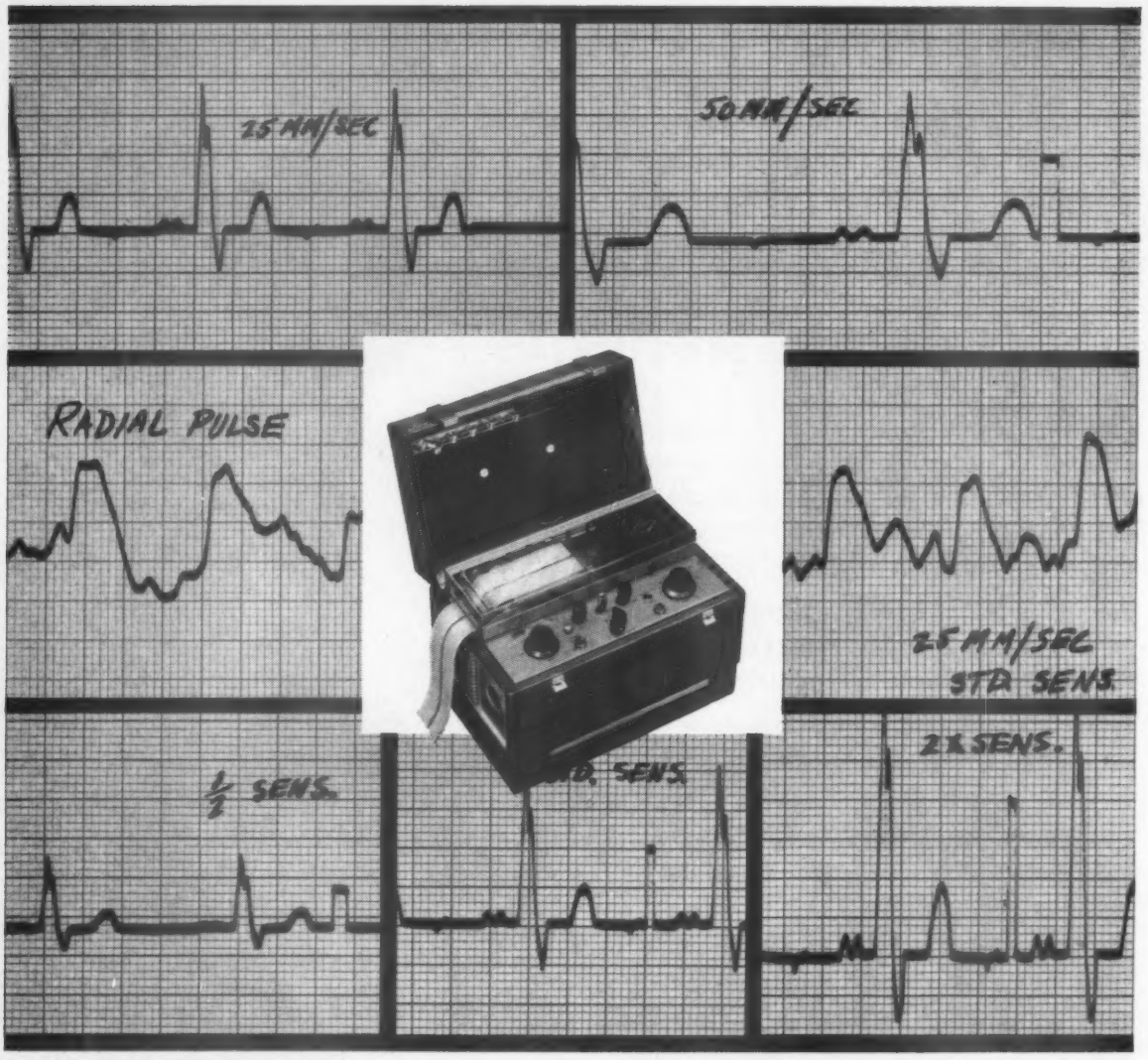
ISORDIL*

Isosorbide Dinitrate, Ives-Cameron

IVES

IVES-CAMERON COMPANY • New York 16, N.Y.

*Trademark



2 CHART SPEEDS • 3 SENSITIVITIES • RECORDING OTHER PHENOMENA

the work of

one SANBORN electrocardiograph

IF you would like the greatest possible versatility in a precision, highly developed ECG, the Model 100 Viso-Cardiette offers many diagnostic and operating advantages to your practice. As illustrated, waveforms may be recorded at the chart speed and sensitivity most suitable for maximum clarity, and non-cardiographic inputs can be either recorded or monitored by using the "100 Viso" in conjunction with other equipment. This modern Sanborn ECG also incorporates fully automatic stylus stabilization as leads are changed, pushbutton "grounding", 8 standard lead positions.

The same instrument is also available in a mobile cabinet of mahogany or rugged, scratch-and stain-resistant plastic laminate, as the Model 100 M. A third Sanborn ECG is the 18 lb. brief case size Model 300 Visette — true portability for any nurse or physician. Call any Sanborn Branch Office or Service Agency for demonstrations or descriptive literature.

SANBORN COMPANY

MEDICAL DIVISION

175 WYMAN ST., WALTHAM 54, MASS.

Schering

SCHERING writes a new chapter in diuretic & hypertension therapy

lowest dosage – unexcelled diuretic activity

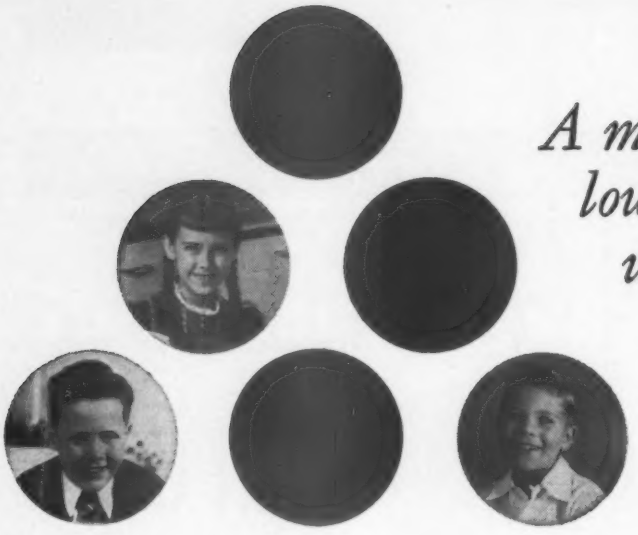
Naqua™

trichlormethiazide

selective electrolyte screening

lower potassium excretion, less risk of digitalis toxicity...maximum sodium output... balanced sodium and chloride excretion...24-hour effect on one 4 mg. dose...significant antihypertensive effect alone, potentiates other antihypertensive drugs...
more economically priced...dosage less than 1/100 of chlorothiazide
Packaging: NAQUA Tablets, 2 and 4 mg. scored, bottles of 100 and 1000.

8-879



A moderate low-fat well-balanced breakfast for children 10-12 years of age

It has been found that those who develop obesity in childhood appear to have more of a dietary problem than those who develop obesity in the adult years. As a service to those advising about the obese child, a basic cereal and milk breakfast is worth consideration. *Its fat content of 10.9 gm. provides 20 per cent of the total calories, thus it is moderately low in fat.* It is well-balanced as shown in the chart below. The Iowa Breakfast Studies demonstrated that children of about this age have better grades and attitudes at school when they eat a *well-balanced* basic cereal and milk breakfast each morning.

Recommended Daily Dietary Allowances and the Nutritional Contribution of a Basic Cereal and Milk Moderate Low-Fat Breakfast*

Menu: Orange Juice—4 oz.;
Cereal, dry weight—1 oz.;
Whole Milk—4 oz.; Sugar—1 teaspoon;
Toast (white, enriched)—2 slices;
Butter—5 gm. (about 1 teaspoon);
Nonfat Milk—8 oz.

Nutrients	Calories	Protein	Calcium	Iron	Vitamin A	Thiamine	Riboflavin	Niacin equiv.	Ascorbic Acid
Totals supplied by Basic Breakfast	503	20.9 gm.	0.532 gm.	2.7 mg.	588 I.U.	0.46 mg.	0.80 mg.	7.36 mg.	65.5 mg.
Recommended Dietary Allowances—Children, 10 to 12 Years (36 kg.—79 lb.)	2500	70 gm.	1.2 gm.	12 mg.	4500 I.U.	1.3 mg.	1.8 mg.	17 mg.	75 mg.
Percentage Contributed by Basic Breakfast	20.1%	29.8%	44.3%	22.5%	13.1%	35.4%	44.4%	43.3%	87.3%

Cereal Institute, Inc.: Breakfast Source Book. Chicago: Cereal Institute, Inc., 1959.

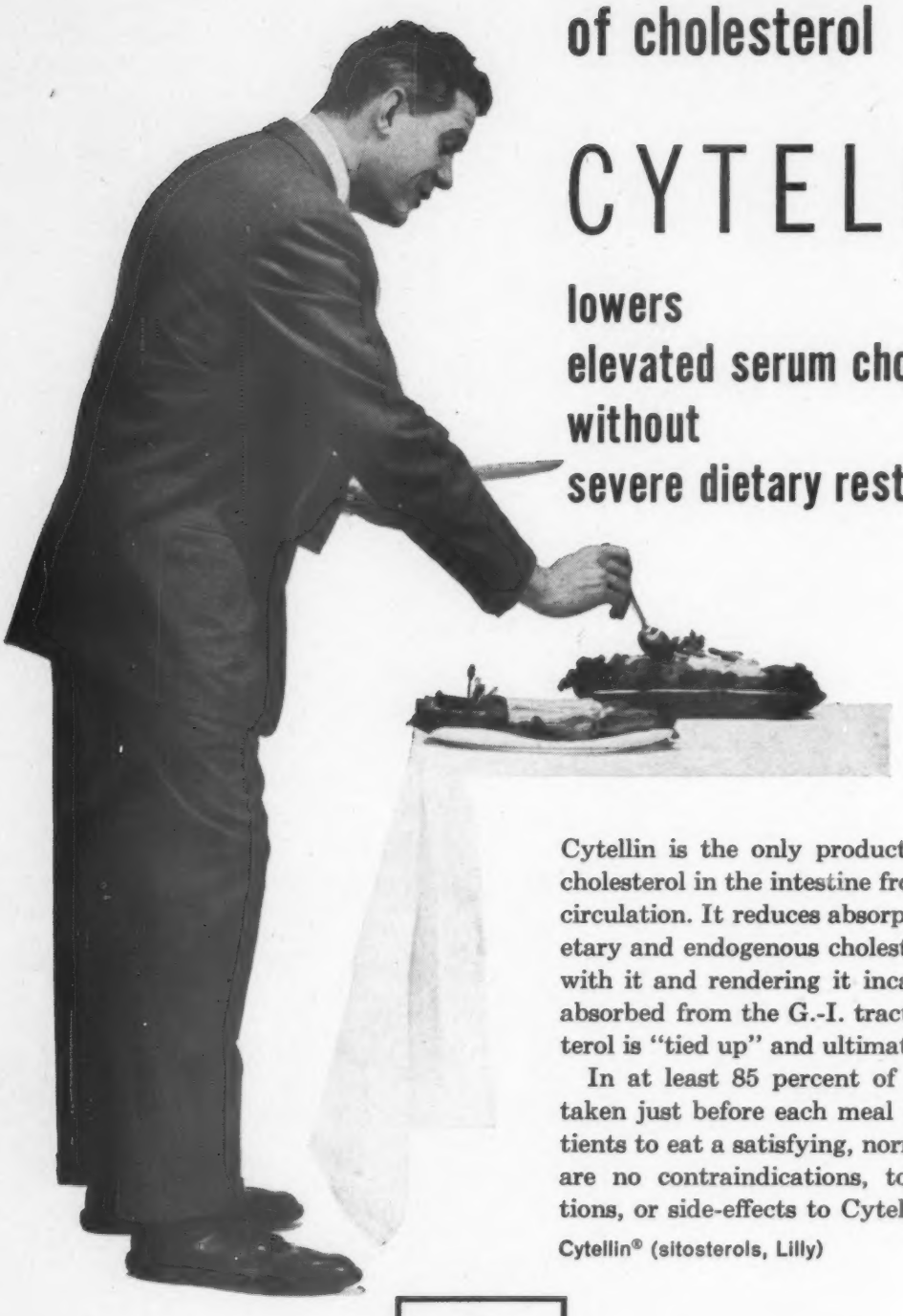
Food & Nutrition Bd.: Recommended Dietary Allowances, Revised 1958. Natl. Acad. Sci.—Natl. Research Council Publication 589, 1958.

Watt, B. K., and Merrill, A. L.: Composition of Foods—Raw, Processed, Prepared. U.S.D.A. Agriculture Handbook No. 8, 1950.

**The allowance levels are intended to cover individual variations among most normal persons as they live in the United States under usual environmental stresses. Calorie allowances apply to individuals usually engaged in moderate physical activity. For office workers or others in sedentary occupations they are excessive. Adjustments must be made for variations in body size, age, physical activity, and environmental temperature.*

CEREAL INSTITUTE, INC.
135 South La Salle Street, Chicago 3

A research and educational endeavor devoted to the betterment of national nutrition



blocks absorption of cholesterol

CYTELLIN®

lowers elevated serum cholesterol without severe dietary restrictions

Cytellin is the only product that prevents cholesterol in the intestine from entering the circulation. It reduces absorption of both dietary and endogenous cholesterol by uniting with it and rendering it incapable of being absorbed from the G.-I. tract. Thus, cholesterol is "tied up" and ultimately eliminated.

In at least 85 percent of cases, Cytellin taken just before each meal will permit patients to eat a satisfying, normal diet. There are no contraindications, toxic manifestations, or side-effects to Cytellin.

Cytellin® (sitosterols, Lilly)

Lilly
QUALITY / RESEARCH / INTEGRITY

ELI LILLY AND COMPANY
INDIANAPOLIS 6, INDIANA, U. S. A.
073061

The American Journal of Cardiology

VOLUME VI JULY 1960 NUMBER 1

Symposium on Cardiology in Aviation

Introduction

ON NOVEMBER 12 and 13, 1959, the first International Symposium on Cardiology in Aviation was held at the USAF School of Aviation Medicine and The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas. This preceded the formal dedication of the new facilities of the Center provided to study the biomedical aspects of aerospace flight.

Cardiology in aviation became important in World War II. High performance aircraft carried man to new heights and greater speeds. Hypoxia and increased gravitational force (g) due to acceleration in combat maneuvers created major stresses upon the circulatory system. The limits of human tolerance to hypoxia and g force were studied intensively. New protective equipment was developed. Because of the nature of flight it was obvious that even momentary malfunction of the circulatory system could not be tolerated. Momentary circulatory collapse during flight could only lead to an aircraft disaster. The physician had to go beyond the question of the presence or absence of disease and assess the performance capability of the aviator. As aviation has progressed, the responsibility of the aircrew has continued to increase. At the threshold of man's conquest of space, the responsibility of the human occupant in the space craft has reached the ultimate. At this historic beginning of the space age, it seemed advisable to assess past experiences in aviation cardiology and define some of the problems indigenous to the new age.

Finest and most dependable performance of aircrews for commercial airlines is of no less importance than military aviation. Today's cardiologist must be able to advise his patients concerning air travel. Unjustified fears of air travel have resulted in the past in mistaken advice to patients with cardiac disease who travel by land over mountainous routes higher in altitude than the altitude in the cabins of commercial aircraft. Similarly, the physician should understand the necessity for complete assessment of the patient's pulmonary, hematologic and metabolic status prior to giving an opinion concerning whether he should or should not fly.

Important studies of the past include the cardiovascular studies begun in World War II by the Royal Canadian Air Force on all entrants into the aviation program. Similarly, the U. S. Navy studied 1,000 healthy young aviators entering training. On April 4, 1957, the U. S. Air Force became the first branch of our Armed Forces to require routine electrocardiograms on all flying personnel. Subsequently, the Federal Aviation Agency has required that all commercial airline pilots have similar examinations.

The first 67,375 electrocardiograms obtained in the USAF program have been analyzed in detail and are presented as part of this Symposium. A large number of the subjects presenting with electrocardiographic abnormalities have been evaluated clinically. Much new information has been obtained in this survey. For the most part previous data on electrocardiography have been obtained from patients in hospitals and clinics who seek medical counsel because of symptoms of disease. Such information is based upon a preselected population and

often gives false impressions concerning the significance of electrocardiographic findings. A good example is the reported high incidence of paroxysmal tachycardia in the Wolff-Parkinson-White syndrome which is not at all comparable to the incidence of this finding in an asymptomatic population. The electrocardiographic data presented in this Symposium provide the basis for future longitudinal studies that will improve medical support for aviation and provide new meaningful data for use in clinical cardiology.

Finally, the study of different measurements in several age groups (sixteen to sixty years of age) suggests that there are clues to aging that may be detected by electrical measurements. Such new data may open new avenues for cardiovascular research.

As the space age blossoms into reality new questions will be posed concerning the influence of the weightless state on the aging process and on the mechanical action of the circulatory system. Will weightless, circulating blood be associated with less vascular disease? What influence will deterioration of anti-g reflexes responsible for peripheral vascular tone have upon hypertension and the sites for the development of atheromatous plaques? These and similar questions will probably be answered within this century.

Just as aviation cardiology has profited from clinical experiences, clinical cardiology can profit from advances in aviation cardiology. Since there is significant difference in the type of population studied, and the challenge is that of a new age, it is hoped that the reader will find this unique Symposium both interesting and informative.

LAWRENCE E. LAMB, M.D., F.A.C.C.
Chief, Department of Internal Medicine
School of Aviation Medicine
The Aerospace Medical Center
Brooks Air Force Base
San Antonio, Texas

Cardiovascular Research in the Public Health Service*

L. E. Burney, M.D.

Washington, D. C.

All of us who are concerned with medicine or aviation, or both, are living in a period more stimulating than any other of living memory. Whether we realize it or not, our age will probably be regarded as one of the greatest scientific revolutions in human history. Speed of innovation is one of the unique characteristics of contemporary science. Another is the increasing synthesis of the biologic and physical sciences in a search for new principles concerning human physiology. These two factors alone present practicing physicians and administrators of medical programs with a problem which has no ready solution; namely, how to keep pace with the rapidly advancing front of science.

The speed of discovery in clinical research is perhaps less difficult to overcome than the increasing dependence of medicine on technics and bodies of knowledge hitherto unknown, or superficially taught, in basic medical curriculums. Hence, the problem of communication between research scientists and medical practitioners involves both enrichment of the physician's basic preparation and his continuing education.

The Public Health Service administers a number of programs which enable us to be of assistance in solving problems of interdisciplinary communication. As a background for my remarks on cardiovascular research, it would be helpful to briefly review our organization.

Organization of Public Health Service

As a constituent unit of the Department of Health, Education and Welfare, the Public Health Service is organized in three operating bureaus and the Office of the Surgeon General, an administrative bureau. The Bureau of Medical Services directly administers our hospitals and medical care programs, including the comprehensive health care of Indians and natives of Alaska. The National Foreign Quarantine Service also is located in that bureau, as well as programs in dental and nursing resources, and administration of the National Hospital and Medical Facilities Construction Program. The latter provides grants to the states for surveys and construction, as well as to non-federal institutions for research in hospital administration. The Bureau of State Services administers our cooperative programs with State Health Departments in numerous fields. It administers our regional organization which provides liasion with the states and with other federal agencies in nine cities, covering the continental United States, Alaska, Hawaii, Puerto Rico and other insular possessions. The Bureau of State Services also conducts important research programs at our Communicable Disease Center in Atlanta, our Sanitary Engineering Center and Occupational Health Laboratory in Cincinnati and the Arctic Health Research Center in Anchorage.

The National Institutes of Health at Bethesda, Maryland, however, is the medical research bureau of the Public Health Service. It has direct responsibility for seven categorical institutes, including the National Heart Institute, a Division of General Medical Sciences, a Division of Biologics Standards and the Clinical Center.

The Clinical Center is a 500-bed research hospital in which the Institutes conduct integrated laboratory and clinical investigations in the following special fields: cardiovascular disease, cancer, neurology, psychiatric disorders, allergy and infectious diseases, and arthritis and metabolic diseases. Patients are admitted to the Center on referral by their physicians and on the basis of relation of their disease to current

* From the Office of the Surgeon General, Public Health Service, U. S. Department of Health, Education and Welfare, Washington, D. C.

investigations. Each Institute conducts additional laboratory and field studies in its special areas of investigation.

The extramural programs of the National Institutes of Health provide financial grants for research and training. These include grants for the conduct of research projects in non-federal, non-profit institutions; research fellowships for the training of promising young scientists in the full range of medical research specialties; and clinical traineeships for physicians in a few specialties, such as cancer and psychiatry. Construction grants are awarded to institutions on a dollar-for-dollar matching basis for the expansion of medical research facilities. In addition, for the past ten years medical and dental schools have received grants to enable them to strengthen their undergraduate and graduate teaching in special fields.

Another illustration of how the Public Health Service assists in research and training is the award of grants for the development of departments of biophysics in medical schools. Two years ago, not more than six medical schools had such departments. Yet, this rapidly growing specialty, pioneered by physicists and biologists in non-medical departments, is destined to provide much of the scientific technic and knowledge essential for the survival of tomorrow's astronauts.

Yet another innovation in research is the establishment of regional university centers on research in aging. The National Heart Institute and the National Institute of Mental Health are jointly supporting two such centers, at Duke University and Albert Einstein Medical College, respectively. The plans of these centers differ according to the geographic and social characteristics of their regions, but both involve an interdisciplinary approach to the basic problems of aging.

National Advisory Councils, composed of leaders in medical research, education and public affairs, assist the Public Health Service in the formulation of policies and the award of grants for each of the programs of the National Institutes of Health. Colleagues from the Department of Defense and other federal medical services serve as ex officio members on all of these councils, along with the leaders from outside the Government.

The total appropriation for the National Institutes of Health for this fiscal year, 1960, amounts to 400 million dollars, a 36 per cent increase over the preceding year. The significance of this increase is, I believe, a reflection of the nation's growing awareness of the scientific and technologic revolutions. In medical research no less than in other scientific fields, American science must hold its leadership. Our medical research and training institutions must be adequately supported to play as dramatic a role of pioneering as developmental research is playing in the launching of space probes. We in the Public Health Service are glad to note that nearly three-fourths (72 per cent) of funds of the National Institutes of Health have been appropriated for aid to research and training in the form of grants and fellowships.

Cardiovascular Research

We are all aware that the answer to questions which confront cardiologists in their daily practice will come from a wide variety of scientific disciplines, and from some investigations which appear at first glance to be remote from the human cardiovascular system. The National Heart Institute is the Public Health Service's focal point for stimulating research interest in this broad field, as well as for the planning of future developments and for the conduct of our own intramural investigations.

The range of work in progress in the nation's public and private non-profit institutions and the forward thinking of the nation's scientists, together illustrate forcefully the new synthesis of biologic and physical sciences. In fields directly or remotely related to heart disease, significant studies range from the development of new instrumentation for the study of the human heart to basic chemical and biologic studies of lower forms of life.

Some of this work unites the interests of space medicine and earth medicine, each profiting in the exchange. Of particular interest to aviation medicine are the attempts to adapt telemetering methods to the study of patients with heart disease in their normal settings. How to determine the capacity for work of a patient with heart disease has long been a major medical problem, especially for the industrial physician.

Some progress has been made in telemetering in the diagnostic laboratory setting. These methods have not been developed to the point that the physician can be provided with a long term measurement of the patient's cardiac pattern. The research problem is to adapt present equipment so that it provides a true record of deviations, rather than a record of a discrete

time and place. For example, scientists interested in instrumentation see no reason why patients could not be given small transistor cardiographs to wear continuously without inconvenience. The machine could be equipped with a selective device that would present the physician with the significant portions of the record.

Those daring scientists who are involved in space exploration have entirely new approaches, new ways of looking at the universe and at the human organism. They want to know, for example, the effects of microclimatic factors on persons adapted for life in macroclimates. In meteorology alone, there have been tremendous advances in measurement so that we are better able to describe climate; but we have scarcely begun to describe the effects of the microclimate of a space probe, a jet plane, a submarine or an air-conditioned building on living organisms over long periods of time. The problems posed by space medicine are formidable; their solution we do not doubt. In those solutions, we will find answers to many questions in the field of cardiology.

One of the ways to speed these solutions is to seek out the imaginative scientists who are motivated to be pioneers and give to them opportunities to combine their specialized talents and skills in fresh approaches to old and new problems. Public Health Service research and training programs are trying to accomplish just such an objective. The young scientists who are brought together now from various parts of a university to study problems in cardiology will be the discoverers and the teachers of tomorrow.

The National Advisory Heart Council is keenly interested in the possibilities of developing such nuclei of interdisciplinary research and training related to cardiovascular disease. A considerable amount of fascinating work, combining physical biology, biochemistry and comparative anatomy, is already being supported by the National Heart Institute.

In studies of lower forms of life, biologists are providing medical scientists with new leads to research on the processes of aging and on human cardiology. For instance, Carroll Williams at the Harvard Biological Laboratory, has discovered a "status quo" hormone in insects which regulates the precise timing that enables them to develop from pupa to imago. As may be surmised, it was a distinct accomplishment to get this microscopic substance into a test tube. The relation of this hormone to the function of the thymus in human beings is of direct concern to medical scientists interested in aging as a biologic phenomenon. Such contributions as these will eventually lead to practical measures for better management of aging in the human patient.

Recent studies of the vascular system of the octopus, also supported by the National Institutes of Health, have been of great interest. Here is an animal known to have adapted to both an aerobic and an anaerobic environment. What happens when it goes to the bottom of the ocean remaining for long periods under great pressure? It has been found that its heart stops and shifts to a metabolism suited to this anaerobic environment. When it "comes up for air," its heart starts again and it shifts back to its aerobic metabolism. The question now is what biophysical, biochemical devices permit this extraordinary shift. Perhaps in earlier periods medicine would not have been interested in this biologic curiosity. As man prepares to launch into space, to remain in submarines at new underwater depths, medical research is compelled to take an interest. What nature has provided, man will learn to imitate in his efforts to master not only his natural environment, but also the microcosmic environment of his new inventions.

These less well publicized types of cardiovascular research illustrate the directions in which science is leading us along unexplored paths to a better understanding of man and his diseases. The National Heart Institute continues to conduct and support a great deal of basic and clinical research directly related to specific cardiovascular diseases.

Improved understanding of the human cardiovascular system and its response to drug therapies is coming from various institutions in studies supported by the National Institutes of Health, as well as from its own laboratories. It is now possible, for example, to observe coronary artery circulation under the image amplifier fluoroscope with high speed photography. By the use of a small plastic catheter inserted into the coronary artery via the artery in the arm, a small amount of radiopaque dye can be injected into the right or the left coronary artery, outlining the vessel's pattern and localizing the site of occlusion. The effect of drugs on coronary blood flow can also be studied and even direct introduction of enzymes to dissolve clots is being tested. Recently, an electronic computer was

adapted to this procedure whereby two pressure measurements are integrated, yielding a measure of instantaneous velocity of blood flow throughout the heart cycle.

The Institute has supported and conducted intensive programs of research on atherosclerosis, with special reference to diet as a factor in its etiology. A summary of nationwide research in this field over a ten-year period has been prepared and published by the Institute.[1] Although there has been much progress, this summary shows the gaps that still remain in our knowledge of this complex disease.

The most fruitful area of research at the present time appears to be in studies of the biochemical mechanisms by which the body handles fatty substances. As a part of its program, the National Institutes of Health has stimulated the use of improved gas chromatography in the analysis of various fats. Recently, the Institute developed a highly sensitive and reliable device which makes it possible to separate and identify the components of fat mixtures in minute samples. Heretofore, the ability of gas chromatoggraphy to differentiate components of natural fats has been limited. Since each component may be metabolized by a different biochemical reaction, research on the role of fatty substances in the etiology of atherosclerosis has been hampered. The use of this new technic should open the way to more rapid progress in knowledge of the disease.

Basic biochemical and clinical investigations at the Institute have made important contributions to the treatment of hypertension. Clinical findings indicate that enzyme inhibition represents a promising new approach to more successful treatment of hypertension, as well as opening the door to increased understanding of the way in which the nervous system chemically influences blood pressure. The National Heart Institute is also making significant contributions to the development of surgical therapy of heart disease, particularly in the areas of diagnostic and evaluative procedures.

For the last ten years, the National Heart Institute has been conducting a long term epidemiologic study of cardiovascular disease in an adult population group. This field investigation was carried out in cooperation with the State and local health departments at Framingham, Massachusetts. Although our investigators focused their study on coronary heart disease and hypertension, these approaches also yielded significant findings on rheumatic heart disease and certain non-cardiovascular conditions. Outstanding characteristics of the study have been the comprehensiveness of medical examinations made of all subjects and the high proportion of clinical followup. The findings contain much of interest on age incidence, sex differential and association of arteriosclerotic heart disease with such factors as obesity, high blood pressure and hypercholesteremia. Several important reports based on data accumulated in the study have been published.[2–4]

One by-product of particular interest to aviation medicine is a report on the electrocardiogram in neurocirculatory asthenia or anxiety neurosis. The question has often been raised as to whether or not anxiety neurosis might be a cause of electrocardiographic abnormalities. Doctors Kannel and Dawber of the Framingham Study and Dr. Mandel E. Cohen of Harvard Medical School compared the electrocardiograms of about 750 healthy control subjects with those of 203 patients who had neurocirculatory asthenia but no cardiac disease or hypertension. All subjects had been studied under identical laboratory and clinical conditions. The investigators concluded[5] that there is no characteristic electrocardiographic abnormality associated with neurocirculatory asthenia, and that abnormalities characteristic of heart disease do not occur as manifestations of neurocirculatory neurasthenia. In short, the electrocardiogram can still be regarded as an objective indicator of heart disease in many cases. Specific electrocardiographic abnormalities cannot be attributed to anxiety neurosis.

In addition to the publication and distribution of research findings from its own investigations, the National Heart Institute assists in improving communication between scientists and medical practitioners in other ways. It supports scientific conferences on general and specific subjects in the field of cardiology. About a year ago, for example, the meeting of the International Committee on Blood Clotting Factors in Rome was made possible by a Public Health Service grant. The National Heart Institute also conducts symposia on various problems in cardiovascular research. For example, owing to the resurgence of interest in epinephrine and its chemical relatives including serotonin, a symposium was held on this subject last year to bring together information concerning these substances and their relation to the mechanism of action of tranquilizers in the treatment of hypertension and some mental disorders.

The research programs of the Public Health Service are designed to stimulate and augment scientific effort in all fields related to human health. One of the underlying purposes of our programs is to enhance the knowledge and skills of medical practitioners. In cardiovascular research as in other areas, we seek the interest and cooperation of physicians as individual practitioners and as members of professional associations.

References

1. Sherman, M. Diet, Hormones, and Atherosclerosis. A Review of Research Grants Supported by the National Heart Institute, Fiscal Years 1949–1958. Washington, D. C., 1959. Government Printing Office.
2. Dawber, T. R., Moore, F. E. and Mann, G. V. Coronary heart disease in the Framingham study. II. *Am. J. Pub. Health*, 47: 4, 1957.
3. Dawber, T. R., Kannel, W. B., Revotskie, N., Stokes, J., Kagan, A. and Gordon, T. Some factors associated with the development of coronary heart disease. *Am. J. Pub. Health*, 49: 1349, 1959.
4. Kagan, A., Gordon, T., Kannel, W. B. and Dawber, T. R. Blood pressure and its relation to coronary heart disease in the Framingham study In: Hypertension, vol. VII, p. 53. New York, 1959. American Heart Association.
5. Kannel, W. B., Dawber, T. R. and Cohen, M. E. The electrocardiogram in neurocirculatory asthenia (anxiety neurosis or neurasthenia): a study of 203 neurocirculatory asthenia patients and 757 healthy controls in the Framingham study. *Ann. Int. Med.*, 49: 1931, 1958.

Influence of Aerospace Flight on the Normal Cardiovascular System

Stresses and Effects*

LAWRENCE E. LAMB, M.D., F.A.C.C.
San Antonio, Texas

When the key to further progress in scientific achievement becomes dependent upon biologic adaptability, it is necessary for us to take stock of our basic knowledge of the vital functions of the human organism. At the threshold of man's conquest of space, one of the vital functions, the circulatory system, may well prove to be the determining factor of man's success or failure. In man's primitive flight into the earth's atmosphere, it was recognized that this unnatural envionment created many stresses affecting the cardiovascular system; for example, both increased gravitation force (g) and hypoxia caused major alterations in cardiovascular dynamics. For this reason, much investigation has been directed toward the study of the influence of the stresses of flight upon the circulatory system.

HYPOXIA

One of the common stresses imposed by aerospace flight is hypoxia. Without protective equipment or other sources to supply oxygen, man usually cannot tolerate altitudes in excess of 23,000 feet. It is interesting to note that the heart muscle itself, however, is relatively resistant to hypoxia. The heart can survive for long periods of time when exposed to an oxygen tension as low as 15 mm. Hg, or to altitudes of 32,000 to 40,000 feet.[1] Survival of the heart muscle does not mean that it remains functional. Under such a degree of hypoxia, the heart will not work under a load or function as a pump for more than about thirty minutes until cardiac failure occurs.

Most instances of circulatory collapse secondary to hypoxia are brought about by reflex action rather than myocardial hypoxia. Circulatory collapse, in turn, causes ischemia and asphyxia of the central nervous system, resulting in loss of consciousness and death.

The normal cardiac muscle differs from all other types of muscle in that it is capable of utilizing lactic acid in its metabolic cycle.[2] Prevention of accumulation of lactic acid, in turn, prevents acidification of heart muscle. Even when the oxygen saturation of the coronary blood is as low as 25 per cent, lactic acid is still absorbed from the blood stream by heart muscle. For this reason cardiac muscle can function for hours at extreme altitudes of 32,000 to 40,000 feet until myocardial function ceases from exhaustion.

Cardiac Adjustments to Moderate Altitude: In the initial phase of flight, exposure to moderate altitude imposes no major stress upon the normal cardiovascular system. Adaptation is accomplished by increased ventilation which maintains a physiologic alveolar pO_2. Although considerable variation is present, most normal subjects will begin to make both pulmonary and circulatory adjustments to altitudes between 6,000 and 10,000 feet. Above these altitudes, the respiratory system has increasing difficulty in maintaining sufficient alveolar pO_2. As a result, the diminished oxygen supply to the circulatory system requires greater adjustment in circulatory dynamics. At first this is accomplished by increased cardiac rate, and in some instances, increased stroke volume. Peripheral vascular dilatation may occur so that a greater amount of oxygen can be absorbed from the blood stream at the level of the tissues. With progressive hypoxia, diminished alveolar

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

oxygen content may result in continued loss of peripheral vascular tone, which eventually may lead to circulatory collapse not dissimilar from common vasodepressor syncope. When this occurs it is usually at altitudes of between 18,000 and 23,000 feet.

As alveolar oxygen diminishes, the amount of oxygen carried by the blood stream decreases. The decreased oxygen content requires an increased cardiac output if adequate oxygen is to be supplied to the tissues. A greater amount of oxygen can also be extracted from the blood stream and, within limits, this aids in compensating for exposure to altitude. While the normal heart muscle will tolerate the increased work imposed upon it by moderate degrees of hypoxia, the situation is quite different in cardiac disease. Whereas hypoxia stimulates dilatation of the normal coronary artery, this cannot be expected when the coronary vessel is rigid from atherosclerosis. Under these circumstances, the increased cardiac work can cause relative coronary insufficiency.

Cardio-inhibitory Response to Hypoxia: After the initial phase of increased cardiac rate, hypoxia may cause cardiac slowing. As hypoxia progresses, it results in stimulation of all the receptors in the brain. Since the dominant influence on cardiac rate is transmitted by the parasympathetic system, cardiac inhibition occurs. Cardiac slowing to the point of collapse due to bradycardia may ensue. Evidence that such cardio-inhibitory responses are in fact due to reflex mechanisms has been adequately demonstrated by classic experiments utilizing sectioning of the vagus nerve.[3] The dominant autonomic control of peripheral vascular tone is mediated by the sympathetic nervous system. In generalized stimulation of all cardiovascular centers, a rise in blood pressure is common. This is caused by increased sympathetic control of the peripheral vascular bed with increased peripheral resistance. Finally, as hypoxia is continued to the point that there is an accumulation of metabolites at the level of the tissues, these influences override sympathetic control and peripheral vascular collapse may ensue. In this manner hypoxia may induce bradycardia with circulatory collapse.

The critical alveolar pO_2 level is 30 mm. Hg. At this level, the oxygen pressure of the venous blood of the central nervous system is approximately 19 mm. Hg. This threshold occurs at an altitude of approximately 23,000 feet. Although there is considerable variation, this is about the lethal altitude for most subjects.

Other Factors Affecting Tolerance to Hypoxia: Whether or not a given degree of hypoxia encountered during flight will seriously affect circulatory dynamics depends on many other factors. Simple decrease in the oxygen content causes a moderate increase in cardiac output. Not infrequently the aviator is also exposed to a considerable amount of heat. This may occur in the plane, waiting for take-off or in certain types of aircraft as a result of the pressure suit and protective equipment worn. The increased environmental temperature increases the demands on the circulation and compounds the effects of hypoxia. Physical exertion increases the metabolic demands of the tissues and requires an increased cardiac output to meet these demands. Man's tolerance to hypoxia is understandably less if physical exertion is required during exposure to altitude. Any factor which increases the metabolic level decreases man's tolerance to hypoxia because of multiple demands upon the circulatory system.

Alterations in the ability of the blood stream to carry oxygen will affect tolerance to altitude. Since each gram of hemoglobin combines with 1.34 cc. of oxygen, a decrease in available hemoglobin will diminish the oxygen content, resulting in increased cardiac output and diminished tolerance to hypoxia. This situation can occur in the presence of anemia or by establishing a carbon monoxide bond with hemoglobin when a person is exposed to carbon monoxide.

Certain diseases of the lung prevent adequate alveolar ventilation and/or diffusion of oxygen into the blood stream. This results in inadequate saturation of the blood stream with a secondary increase in cardiac output. The difficulty is compounded during exposure to altitude. Hypoxia can also cause dramatic increases in pulmonary hypertension which may precipitate right heart failure.

Arrhythmias During Hypoxia: Although many simple cardiac arrhythmias are not associated with either cardiac disease or significant alteration in cardiovascular dynamics at ground level, they may induce serious arrhythmias during hypoxia. An ectopic ventricular focus which may cause only occasional ventricular premature contractions during normal cardiac rhythm may assume control of the heart during inhibition of the sinus pacemaker due to reflexes initiated during hypoxia. If the ventricular focus is rapid, ventricular tachycardia

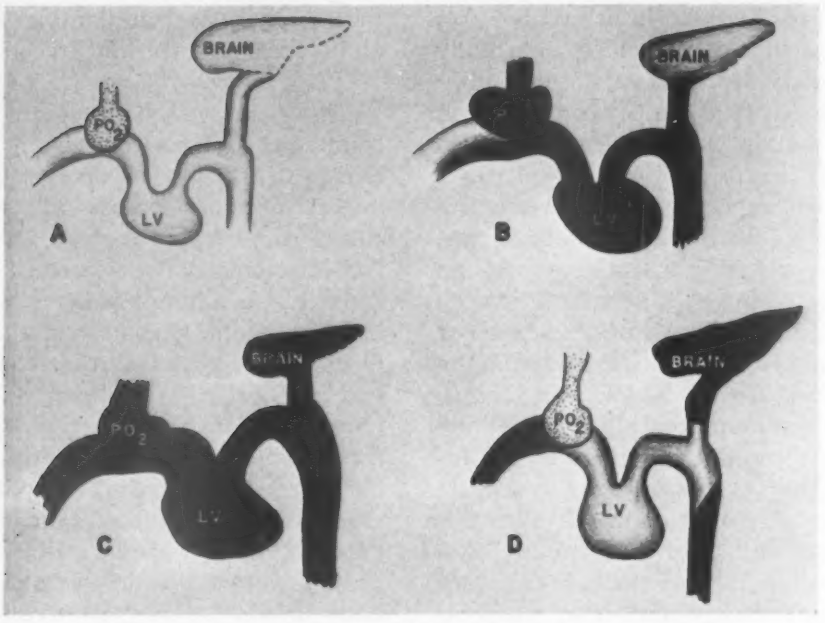


FIG. 1. A, in normal circumstances oxygen is transported from the lung to the brain in the time required for circulation between the lung and brain (lung-to-brain circulation time). B, with explosive decompression oxygen leaves the blood stream to escape through the lung and the blood leaving the lung is essentially anoxic. C, the anoxic blood reaches the brain within the lung-to-brain circulation time. After the anoxic blood reaches the brain the tissue oxygen reserve begins depletion. D, the brain remains inadequately oxygenated until lung-to-brain circulation time has elapsed to bring oxygen to the brain after oxygen inhalation is resumed.

may occur. Similarly, ectopic foci in the atria may become the primary pacemaker when the usual order of excitation is disturbed. Responses such as those discussed require evaluation by a dynamic physiologic approach of individual adaptation to the stresses of aerospace flight in contradistinction to the more elementary problem of determining only the presence or absence of cardiac disease.

Acute Anoxia

One of the interesting features of anoxia is directly related to circulation time. This is the time reserve, or time of consciousness noted when a person is suddenly exposed to altitudes of 50,000 feet or above.[4–8] This may occur when it is necessary to bail out at high altitudes, or when there is sudden loss of pressure in the cabin during a high altitude flight. The alveolar gases are rapidly expelled to the external environment of markedly diminished ambient pressure, and for circulatory purposes, the alveolar sac is anoxic. In fact, the oxygen tension of blood going to the lungs is momentarily greater than the pressure of the oxygen within the alveolus. Oxygen rapidly diffuses out of the venous blood into the anoxic alveolus. The blood which leaves the lungs is relatively unsaturated with oxygen. Consciousness, however, will be maintained until after the anoxic blood reaches the brain. The circulation time from the lungs to the brain is seven to ten seconds. The oxygen tension within the brain cells will then be depleted. This requires four to six seconds. Thus, a total of only ten to fifteen seconds of consciousness can be expected under these circumstances (Fig. 1).

If the period of exposure to extreme altitude is less than ten to fifteen seconds, a short period of unconsciousness will still occur during the time that relatively anoxic blood bathes the cells of the brain. Transitory loss of consciousness can be avoided only when exposure is less than five to six seconds or within the time limit that the cells of the brain can function on intracellular oxygen.

At lower altitudes, the time reserve is extended until the oxygen within the alveolus is depleted. In both cases, however, loss of consciousness will ensue within ten to fifteen seconds after the pulmonary blood flow ceases to be adequately oxygenated.

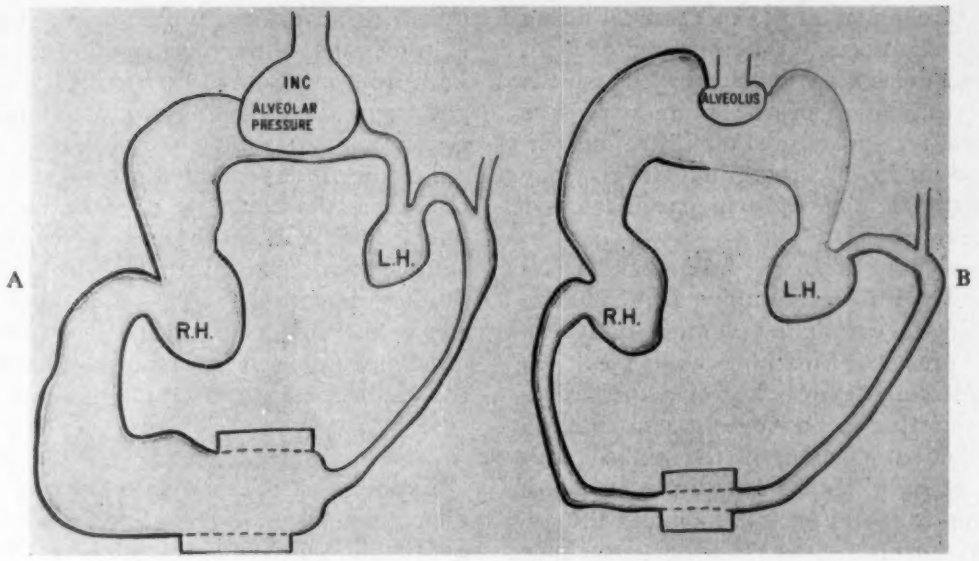


FIG. 2. A, pressure breathing inhibits return of blood to the left heart. B, external pressure on the body with a g suit displaces the circulating blood volume to the pulmonary vascular compartment.

POSITIVE PRESSURE BREATHING

One of the protective mechanisms which can be utilized to maintain the alveolar pO_2 is the administration of 100 per cent oxygen. Man can ascend to an altitude of 33,700 feet breathing 100 per cent oxygen and still maintain a normal alveolar pO_2 of 103 mm. Hg. Above this altitude, respiratory and circulatory adaptations are necessary in order to provide adequate transport of oxygen to the tissues. As a further protective device, controlled positive pressure breathing of oxygen may be utilized. This provides pressure artificially, which would ordinarily be present because of atmospheric pressure at ground level. This, in turn, results in elevation of the alveolar pO_2.

Under normal circumstances, both the systemic and pulmonary circulation are exposed to the same external pressure of 760 mm. Hg at ground level. When the pressure applied to the pulmonary circulation is unequal to external pressure applied to the body or systemic circulation, the mechanics of circulation may be profoundly altered to the point of serious disability. Usually if the pressure applied to the alveolus and the pulmonary circulation does not exceed the pressure applied to the external surface of the body by more than 10 mm. Hg, no particular adverse effects are caused. If the difference in pressure is 15 to 20 mm. Hg or greater, obstruction of the venous return to the heart occurs. There will be a diminution in the blood flow to the lungs and a fall in systemic pressure may occur. The peripheral arterial circulation must contract in order to maintain adequate blood flow to the vital centers. When the disproportion between pressure applied to the pulmonary circulation and the pressure applied to the peripheral circulation reaches the magnitude of 50 to 60 mm. Hg, circulatory collapse will occur (Fig. 2).

Electrocardiographic Changes: Early in the investigation of the influence of pressure breathing on the circulatory system, electrocardiographic alterations were noted. German scientists interpreted T wave changes noted in the electrocardiogram as indicative of relative coronary insufficiency secondary to altered hemodynamics.[9] Because of this observation, the German pilot of World War II was not commonly equipped with pressure breathing equipment. It was thought that the additional altitude which was to be gained by this mechanism was not worth the added danger imposed upon the circulatory system.

Vagal Reflexes: Powerful reflexes may be initiated through simple respiratory mechanics. Stimulation of the lungs may result in secondary vagal responses with cardiac inhibition and vasodepressor responses. Their occurrence may be due to receptors from the lung itself with afferent fibers extending into the vasomotor and cardio-inhibitory centers or there may be intermediate factors such as reflexes with afferent fibers within the heart which are stimulated

as a result of changes in the mechanical filling of the heart chambers. Whether one or both of these mechanisms are involved, the result is the same; stimulation of the pulmonary tree through positive pressure breathing, breath-holding and other breathing maneuvers may result in significant changes in cardiovascular reflex mechanisms.

Changes in Blood Volume: Still another effect of positive pressure breathing is the change in the available circulating volume of blood. Prolonged pressure breathing will result in increased pressure against the venous return to the heart, resulting in pooling of the circulation in the dependent portions of the body. This eventually leads to significant displacement of fluid volume from the vascular bed to the extravascular spaces. One of the protective mechanisms which may be utilized to combat adverse reactions to positive pressure breathing is the g suit. With its use, external pressure may also be applied to the body as well as to the pulmonary circulation. When a helmet and pressure suit are combined, the unit provides a closed pressure system with equal pressure applied to both the pulmonary and systemic circulation. With such protective equipment, the environment within the suit, not the external altitude, is the important factor. Such a suit protects the human occupant and his circulatory system from adverse reactions to otherwise intolerable environments.

Decreased Ambient Pressure

At ground level we are exposed to a constant pressure of 760 mm. Hg, or atmospheric pressure. This pressure diminishes on exposure to altitude. By inhaling 100 per cent oxygen, the influence of hypoxia can be obviated up to altitudes of 33,700 feet. The only significant alteration in environment becomes a decrease in ambient pressure. Below altitudes of 27,000 to 30,000 feet, this has little or no effect on the circulation. When the pressure is decreased to the point that nitrogen fails to remain in solution within the blood stream and other tissues, adverse responses occur. These are not limited to the circulatory system, but may affect any portion of the body. When the central nervous system is involved, cardiovascular reflexes may alter circulatory dynamics similar to the bradycardia sometimes seen in cerebral vascular accidents. Direct impairment of circulation to any of the organs owing to release of gases from solution may produce local symptoms; as an example, pulmonary involvement is associated with chest pain and coughing. Pain from any source due to local formation of gas may induce vasomotor collapse just as may occur with pain from any other cause.

For the aforementioned reasons, the influence of decreased barometric pressure on the circulatory system in the absence of cardiovascular complications has received little attention. Studies indicate that below an altitude of 30,000 feet in the absence of release of dissolved gases, circulatory dynamics, orthostatic tolerance and the electrocardiogram remain unaltered.[10,11]

Influence of g Forces

Exposure of the human subject to increased g force produces adverse effects to a large extent by affecting circulatory dynamics. The effects of g force on the circulatory system depend on the relation of body position to direction of application of force. On Earth, when man is standing upright, his body is under the influence of 1 g, acting parallel to the spine and directed downward. This force of 1 g is responsible for body weight and the weight of the column of blood in the aorta and other vessels. The influence of gravity aids flow of blood down the aorta and to all regions below the level of the aortic valve; it impedes the flow of blood upward toward the head. The pressure created by systolic contraction results in a greater perfusion pressure in the lower extremities than in the brain.

Effect of Increased G Loads on Brain and Eye Perfusion Pressures: The effect of the weight of the blood column upon blood pressure can best be understood by a simplified mechanical analogy. Let us assume that the blood pressure at the aortic valve is 124/84 mm. Hg, and the distance between the aortic valve and the base of the skull is 30 cm. (Fig. 3). A column of blood 30 cm. high will exert a pressure of 24 mm. Hg under the influence of 1 g. In our analogy the perfusion pressure at the base of the skull will only be 100/60 mm. Hg (124/84 − 24 mm. Hg). The eye has an average internal pressure of 30 mm. Hg; thus an arterial pressure of over 30 mm. Hg at eye level is necessary to establish a pressure gradient permitting perfusion of the fundi. The pressure gradient for the eye in the example is only 70/30 mm. Hg (100/60 − 30 mm. Hg).

In aerospace flight, it is common to expose the aviator to acceleration force which acts as g force. This is especially common in combat

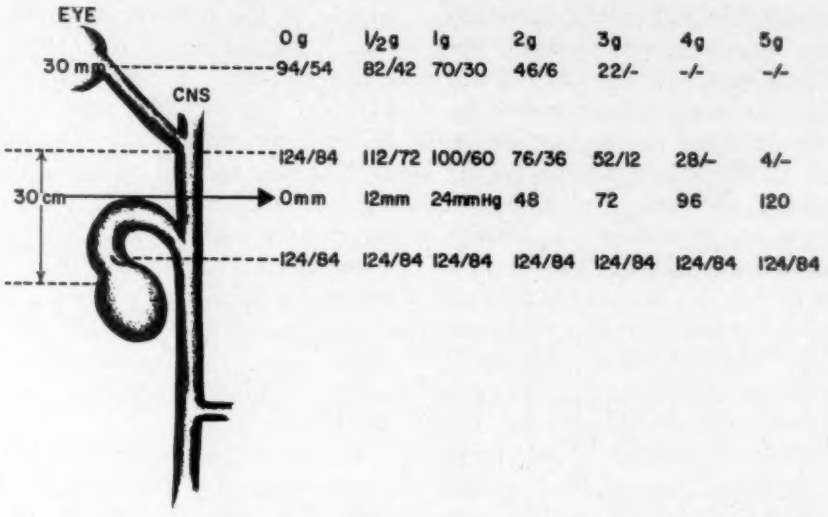


FIG. 3. Perfusion pressure for circulation to the brain and eye is markedly affected by g force with the subject in the upright position. The change in perfusion pressure with differing amounts of g force is depicted above. Note that during zero g the column of blood is weightless; thus one expects a greater perfusion pressure to the head when orbital velocity is reached during space flight.

maneuvers and will be a major stress in future rocket flight. Acceleration increases g load in excess of the force encountered at ground level, which affects the mechanics of circulation to the point of circulatory collapse. Utilizing the mechanical analogy one can see how g forces produce symptoms by their effects on the circulation. With the upright subject exposed to a 2 g force, the weight of the 30 cm. blood column will be doubled and it will exert a pressure of 48 mm. Hg. The pressure gradient for perfusion of the brain drops to 76/36 mm. Hg (124/84 − 48 mm. Hg). The perfusion pressure for the eye is 46/6 mm. Hg (76/36 − 30 mm. Hg).

As the g load is increased to 3 g, the pressure exerted by the column of blood between the heart and the brain is increased to 72 mm. Hg (24 mm. Hg × 3). The perfusion pressure for the brain falls to 52/12 mm. Hg (124/84 − 72 mm. Hg) and as low as 22/ − mm. Hg (52/12 − 30 mm. Hg) for the eye. Perfusion of the eye is totally dependent on systolic pressure, and the threshold of visual disturbances, secondary to altered circulatory dynamics, is approached.

Under the influence of 4 g, the pressure exerted by the brain-to-heart blood column is 96 mm. Hg. The eyes are no longer perfused with blood and the pressure gradient for perfusion of the brain drops to 28 mm. Hg during systole.

This simple mechanical analogy explains how failure of the circulatory system is responsible for the visual reactions to excess g load. Visual tolerance to g load is usually below 4 g. The peripheral area of the retina is naturally the most distal area to perfuse and it is affected first, resulting in loss of peripheral vision. This is followed by loss of central vision, although the subject maintains consciousness.

At a level of 5 g, the heart-to-brain blood column exerts a pressure of 120 mm. Hg. To maintain consciousness, blood pressure at the level of the heart must be in excess of 120 mm. Hg.

By using this same mechanical analogy one may appreciate the direction of changes which may be encountered during space flights and on arrival at other planets. Once the vehicle has reached orbital velocity, and the weightless state occurs, the column of blood between the heart and brain will exert no pressure, even in the upright position. This will result temporarily in an increased distribution of blood to the brain, and a low grade carotid sinus stimulation. At arrival on the Moon, man will be exposed to a gravitational field of one-sixth that of Earth. The difference in pressure between the heart and the brain drops to approximately 4 mm. Hg. Increased blood flow to the upper portion of the body will probably result in relaxation of reflex peripheral vascular tone to maintain normal distribution of blood volume.

This illustration is a simple mechanical

analogy and considerable individual variation exists. The short squat person is more resistant to the circulatory effects of g load, since the heart-to-brain blood column is shorter. Various maneuvers designed to decrease excessive flow of blood to the lower portion of the body protect against deficient circulation to the brain. Circulatory dynamics are usually adequate to maintain function for several minutes at levels of 3.5 g. At a level of 5 to 6 g, human tolerance is usually less than one minute. Since the various tissue cells have adequate oxygen scores within the cell to maintain function for very short periods of time, the human body is able to withstand a very large g force for a very short duration of time, usually less than two seconds.

The critical factors of circulatory perfusion of the vital organs become even more important as the speed of aerospace vehicles is increased. Maneuverability at high speeds is ofttimes a desirable military objective. During maneuvers, the amount of g load applied to the human subject will be dependent upon the velocity squared divided by the radius turn of the vehicle. At Mach 1 or velocity of sound, in order not to exceed 10 g, the loop for a turn must involve a change in altitude of 10,000 feet.

The amount of g load encountered in German fighter craft was determined in World War II and in usual flight patterns, 4.5 to 5 g were sustained for periods of three to five seconds during combat maneuvers. These are usually within tolerable limits. However, g loads greater than this occur not infrequently during acrobatic maneuvers and modern aircraft utilized for these purposes are capable of withstanding much greater g force than the human occupant. It should be equally obvious, particularly in the non-military situation, that aircraft which cannot pull g loads of the magnitudes discussed herein present no major hazard to the normal circulatory system.

Effects of Cardiovascular Diseases: When one considers the mechanics involved in increased g load, it is easy to see why a number of cardiovascular diseases present undesirable circumstances to cope with the change in cardiovascular dynamics. To illustrate, *aortic stenosis*, in which the pulse pressure is relatively small, may not provide sufficient blood pressure for adequate perfusion pressure to the brain. *Aortic insufficiency*, with its marked drop in diastolic pressure provides an even lower threshold for diastolic perfusion of the brain. As the weight of the column of blood increases diastolic regurgitation is increased, creating all its complications. Even small amounts of aortic valvular insufficiency may become significant under increased g load. The increased diastolic overloading further compromises other physiologic adjustments normally needed to adapt to increased g load. The adverse effect of *coronary artery disease* is still another defect which can compromise g tolerance. When cardiac work is increased in the face of diminished cardiac output under g load, relative coronary insufficiency may occur. Anatomic studies have demonstrated this to be a fact.[12]

In the normal subject the blood pressure will be maintained at the level of the heart under g loads of less than 5 g per fifty seconds. Little investigation has been carried out concerning the level of the blood pressure which might be encountered in the presence of the various cardiac diseases mentioned. Usually at the onset of increased g force, there is a drop in pressure within two seconds at the level of the carotid artery. At nine to twenty seconds following the onset of g load, a period of recovery occurs. This is due to the reflex response of pressor sensitive reflexes which augment peripheral resistance. If the g load becomes too great, collapse due to overstress occurs which in effect means that the weight of the column of blood reaches such a level that the heart is no longer able to pump effectively and circulatory collapse ensues. Collapse due to overstress causes severe circulatory alterations and a prolonged period of time is required for recovery.

Other Circulatory Adaptations to Increased G Load: There are a number of other circulatory adaptations which occur under g load with the subject upright. The blood flow to the apices of the lungs is markedly diminished and the apex regions appear translucent on roentgenograms taken during g load. The redistribution of pulmonary blood augments the available venous return to the heart, but at the same time it diminishes perfusion to a portion of the lung field ordinarily utilized for respiration.[13]

Under normal circumstances, the left ventricle does not empty completely during systole. As the work of the heart is increased under g load, systolic emptying becomes more complete and literally no blood remains in the left ventricular chamber at the end of systole. The volume of the left ventricle is likewise contracted. In essence, this represents a more efficient utilization of the volume of blood present in the systemic

arterial circulation. The decrease in the amount of blood in the upper extremities and the apices of the lung and the contraction of the size of the left ventricle are factors which aid the circulatory system in maintaining normal blood pressure at the level of the heart, as well as supplying blood to the vital centers.

As increased g force is discontinued and the period of vagal slowing occurs, or if g force is discontinued by achieving a near weightless state, a redistribution of blood occurs. The heart becomes markedly dilated with expansion of the left ventricle and the pulmonary blood supply to the vascular bed is markedly increased, resulting in pulmonary engorgement.[14]

Increased g force results in a greater intravascular pressure in the dependent portions of the body. This, in turn, causes an increase in the pressure gradient responsible for a diffusion of fluid out of the vascular bed into the extravascular compartment. It is more difficult for fluid to return to the circulating blood volume at the venous portion of the capillary bed. These effects result in the accumulation of extravascular fluid with formation of edema and a decrease in the circulating blood volume.

Changes in Peripheral Resistance: To maintain adequate circulatory dynamics at ground level, it is essential that peripheral vascular tone be maintained when the upright position is assumed. Without adequate vascular tone, the weight of the blood stream will result in excessive pooling of blood in the dependent portion of the body and an inadequate distribution of blood to the brain. This is called orthostatic intolerance, or simply, intolerance to a force of 1 g. A common clinical example is orthostatic intolerance after sympathectomy.

When g force is increased, reflex control of peripheral resistance is essential to maintain adequate perfusion of the brain. As human tolerance to g load is exceeded, the ability to contract the peripheral vascular bed by reflex control is exceeded. Anything which diminishes reflex control of peripheral resistance decreases g tolerance. It is obvious that anyone taking sympathetic blocking agents cannot be expected to have normal tolerance to g load, and cannot perform in military aircraft expected to carry out combat maneuvers. Similarly, heat, early stages of hypoxia and other stresses added to exposure to increased g force decrease g tolerance.

Changes in Cardiac Rhythm: In addition to the simple mechanical influences of increased g force, profound changes in cardiac rhythm in normal subjects have been observed. As the stress is increased, there is an increase in heart rate. This is the sympathetic phase of cardiac acceleration. The pulse rate may reach levels of 160 per minute on exposure to g loads near 4.5 g. Occasionally, higher rates are noted. When the g load begins to decrease, or during the coasting phase of the human centrifuge, the heart rate begins to slow. This is called the period of vagal rebound. In susceptible persons, significant collapse due to bradycardia may occur during this period and immediately after termination of excess g load, particularly if the subject is not immediately removed from the centrifuge,

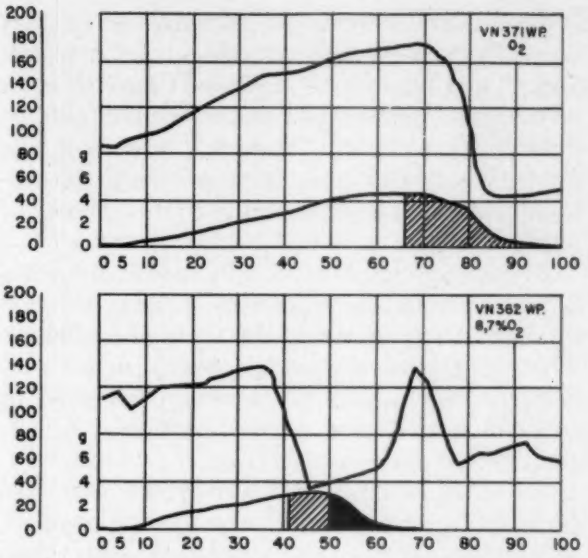


FIG. 4. The upper graph depicts the effects of increasing g load on the pulse rate. The top curve indicates the pulse rate which increases as g load increases. At a peak of 4.5 g (indicated by the lower curve) the pulse rate reaches approximately 180 beats per minute. The time from the onset of increasing g load is indicated at the bottom of the graph. The peak of the accelerated (sympathetic) phase occurs seventy seconds after the gradual onset of increased g load. After this time interval as g load is gradually diminished (the coasting phase of the centrifuge) a precipitous fall in pulse rate occurs to approximately 40 beats per minute. This is the vagal rebound phase following the accelerated or sympathetic phase. In the lower graph the same subject is exposed to hypoxia (breathing 8.7 per cent oxygen gas mixture) and increasing g load. The pulse rate is rapid at the onset of the centrifuge run. As indicated by the pulse curve a precipitous fall in heart rate occurs shortly before the peak of g load (3 g in this case) is reached. The procedure was terminated. The black area under the lower curve as g load was diminished indicates loss of consciousness. The secondary rise in pulse rate is a second period of predominate sympathetic influences following the preceding vagal period of collapse due to bradycardia. This figure is adapted from the work of Gauer.[16]

and permitted motion or other maneuvers that normally protect against orthostatic collapse. Gauer and Wieckert[15] observed marked sinus arrhythmia and displacement of the cardiac pacemaker to the A-V node and bundle of His. Published figures demonstrate ventricular ectopic beats appearing during the phase of marked cardiac slowing.

The marked vagal rebound phase with cardioinhibitory response represents a great increase in vagal tonus following the sympathetic phase when vagal tone was almost non-existent. Accompanying features of increased vagal tonus other than circulatory disturbances may occur; e.g., nausea and hypoglycemia.

When hypoxia is superimposed on exposure to increased g load, adverse responses occur much earlier.[16] Collapse due to bradycardia may occur below 3.5 g. This collapse, not the mechanical aspects of g load, may in this case precipitate loss of consciousness (Fig. 4).

Effect of Body Position: In contrast, in the influence of g force with the subject in the upright position, the distribution of blood to the central nervous system is markedly increased if the human subject is exposed to negative g. An example of negative g occurs if a man is accelerated upward with the head down, when a large volume of blood would be distributed into the carotid arteries and the brain. Because of the numerous vagal receptors in the carotid artery, aortic body and in the central nervous system, the human subject does not tolerate well even small amounts of g force in this direction. For this reason, in aerospace flight it is wise to avoid exposure to g force in this direction whenever possible.

One method of counteracting the adverse circulatory responses to g load is to position the aviator in the transverse position. In this manner, g force is directed perpendicularly to the long axis of the body, and large amounts of g force can be tolerated. However, when g load becomes excessive, respiration becomes difficult owing to the pressure against the thoracic cage and against the abdomen. Circulatory deficiency is merely traded for respiratory impairment. Another type of adverse effect on the circulatory system due to g load is reflex action induced by pain. As g force is increased, the weight of each organ is likewise increased. The pull against the viscera and vital organs stimulates pain receptors which in turn may cause vagal responses.

In order to circumvent the adverse effects of g load on the circulatory system expected during rocket flight, experimental work has been carried out by Clarke et al.[17] with the subject exposed to nearly transverse g load. Subjects were then exposed to three successive peaks of g load comparable to what might be expected during the three stages of rocket flight to orbital velocity. The profiles studied were three successive peaks of short duration of 12 g, 10 g and 8 g. The subjects were inclined 25 degrees forward toward the direction of g force. Peripheral vision was lost at levels of 10 g. Tolerance to 12 g was limited to about five seconds, and to 10 g about thirty seconds. In this position, it appears that most subjects will tolerate a three-stage rocket profile utilizing three successive peaks of 8 g.

Space Flight

Since the inception of aerospace flight to its present state of evolution, man has constantly been required to develop protective mechanisms to prevent adverse cardiovascular dynamics secondary to the stresses of flight. This has been admirably achieved. At each new advance in aviation, however, the amount and type of stress have been progressively increased. By simple reference to the cardiovascular physiologic mechanisms involved, one can see the necessity for adequate circulatory dynamics and a healthy circulatory system as a prerequisite for exposures to the type of stresses which are expected to be encountered in combat aviation. Other problems related to the physiology of the circulatory system include venous status, the influence of cold, psychic stresses and a host of others, all of which have direct effects on the circulatory system.

The influences of prolonged aerospace flight on the circulatory system must now be considered. It is in this area that our knowledge is most deficient. Whereas we know the levels of human tolerance to g force and these can now readily be determined on an individual basis and whereas we have developed protective mechanisms against relative hypoxia and decreased atmospheric pressure, our knowledge of the added effects of relative immobility on the circulatory system such as may be encountered during prolonged space flight is relatively limited. Only a small amount of experience has been gained as the result of experimental work on subjects confined to bed rest. It is a well known clinical observation that after periods of prolonged bed rest, peripheral vascu-

lar resistance is markedly diminished and when the patient assumes the upright posture, circulatory collapse may occur. This is the result of removing the influence of 1 g normally encountered at sea level and directed parallel to the longitudinal axis of the body. In essence, rather than being exposed to longitudinal g as a daily occurrence, the patient at bed rest is exposed to transverse g.

Stresses During Rocket Launching: To outline the problem areas which may be anticipated as the frontiers of aviation progress to include the conquest of space, let us examine the influences which might be anticipated from the time of rocket launching until return to Earth. It is to be expected that a large amount of anticipation, or anxiety, will be present in the subject at the time launching is to begin. This will augment the sympathetic phase of neurogenic control of the circulatory system. At the first stage of the thrust, relatively large g force will be applied to the human subject. During this period, cardiac acceleration will be increased. It is anticipated that the astronaut will be in such a position that the g force will be applied in the most advantageous fashion to the circulatory system, probably in the transverse direction. This, in turn, will produce some impairment of respiration. At the end of the first stage of flight, g force will be markedly diminished for a short period which could permit a vagotonic rebound phenomenon to occur. Following this period, two more stages of exposure to a relatively large g load will occur prior to the time that orbital velocity is reached.

Stresses in Outer Space: Assuming that no adverse responses occur in the nature of vagal rebound phenomenon during either of these stages of rocket propulsion, the astronaut will arrive in outer space in a relatively weightless environment, owing to the relative absence of gravitational force. At this point, the successive stimuli of g load will have been removed and in the absence of even the normal 1 g force, redistribution of blood volume may occur. In a susceptible person, such redistribution of blood volume may well cause excessive stimulation of the carotid sinus mechanism producing significant alterations in cardiovascular reflex mechanisms. A relative bradycardia should be expected as a normal event.

When the point is reached that a satellite can be maintained for prolonged periods of time in outer space with adequate protection for human life, then the additional problems of prolonged confinement or relative immobility must be considered. At present, we have no experimental knowledge concerning how rapidly normal cardiovascular reflexes designed to combat g force will lose their effect in a weightless state. However, from the simple observation of patients at bed rest, it can be assumed that after a week's time in a weightless state the usual cardiovascular reflexes which protect a person against adverse responses to change in body position or other mechanical stresses will have lost a great deal of their normal effectiveness.

Stresses on Return to Earth: As the astronaut begins his return journey to Earth, he may find that his circulatory system is less able to cope with the stresses of living on Earth and, as he is exposed to g load, he may find it relatively impossible to maintain an upright posture or to perform what are normally considered relatively simple tasks. After arrival on Earth from a prolonged period of space flight, the astronaut may require a period of convalescence to adjust to the earth's environment—similar to a period of convalescence expected for any person who is hospitalized at bed rest for a prolonged period of time.

The next large area of research on the physiologic stresses of aerospace flight on the circulatory system must then direct itself toward questions of the influence of the added stress of relative immobility on the circulatory system. Efforts should be directed toward studying means of combating the deleterious effects on the circulatory system of the loss of gravitational force for any prolonged period of time. Approaches to this may well include the creation of artificial g force, certain mechanical devices or some form of change in the pressure suit that will, in effect, constantly stimulate the circulatory system with forces comparable to 1 g as normally encountered at ground level. It is not anticipated that these will be unsurmountable difficulties, but they exemplify once again the influence of stresses of aerospace flight even on the normal circulatory system.

Summary

1. The circulatory system is a transport mechanism and the work imposed on it must consider pulmonary problems as a source of supply, the metabolic demands and the hematologic capability of the blood stream to carry oxygen. All these considerations as well as the heart and blood vessels must be considered in evaluating circulatory responses to the stresses of aerospace flight.

2. Many of the circulatory responses to the stresses of flight are dependent on reflex control. The simple basic reflex mechanisms are discussed.

3. Hypoxia is a common stress encountered in aviation due to exposure to altitude. Heart muscle is unique in its metabolism and is relatively resistant to hypoxia. By contrast, asphyxia, which means retention of carbon dioxide as well as lack of oxygen, is poorly tolerated by the myocardium. Coronary insufficiency is akin to asphyxia, rather than to hypoxia. The mechanics of altered cardiovascular function in hypoxia are discussed as well as certain reflex responses.

4. Explosive decompression or acute anoxia is accompanied by loss of consciousness after a short period of time. The time lag is largely dependent on circulation time between the heart and brain. This time interval is called the time of consciousness.

5. Positive pressure breathing inhibits venous return to the left ventricle and changes the distribution of blood volume. The pressure suit combined with positive pressure breathing tends to create more normal distribution of circulating blood volume and creates a closed environment for the occupant. The influence of pressure breathing on the dynamics and reflex behavior of circulation is discussed.

6. Decreased atmospheric pressure alone has little effect upon circulation unless true decompression sickness (dysbarism) occurs.

7. Increased g force commonly encountered in aerial maneuvers affects the mechanics of the circulation by changing the normal blood pressure relations between heart level and other parts of the body. These mechanical influences are responsible for losses of vision and consciousness encountered in the presence of large g loads. The influence of weightless conditions on blood pressure during space flight at orbital velocity can be predicted by analogy of mechanical principles. The direction of initial changes in blood pressure in the upright human subject on Mars, the Moon and other planets can also be predicted. The best body position for maximum tolerance to increased g load is largely dependent upon mechanical factors.

8. Marked changes in cardiac rhythm as controlled by reflex mechanisms are encountered during the stress from increased g load and immediately following exposure to increased g load. These are discussed in detail.

9. The effects on cardiovascular dynamics of space flight and the importance of maintaining antigravity reflexes during a prolonged period of weightlessness are discussed.

References

1. Kottenhoff, H. Steigerung der Höhenfestigkeit durch Umstellung. *Luftfahrtmed*, 4: 294, 1940.
2. Rühl, A. and Thaddea, S. Anoxie und Milchsäurestoffwechsel von Herz und Lunge. *Naunyn Schmeidebergs Arch.*, 191: 452, 1939.
3. Greene, C. W. and Gilbert, N. C. Studies on the responses of the circulation to low oxygen tension. II. The electrocardiogram during extreme oxygen-want. *Am. J. Physiol.*, 51: 181, 1920.
4. Sweeney, H. M. Explosive decompression. *Air Surgeon's Bull.*, 1: 1, 1944.
5. Benzinger, T. Explosive decompression. In: German Aviation Medicine in World War II, vol. 1, p. 395. Washington, D. C., 1950. Department of the Air Force.
6. Luft, U. C., Clamann, H. G. and Opitz, E. The latency of hypoxia on exposure to altitude above 50,000 feet. *J. Aviation Med.*, 22: 117, 1951.
7. Hall, F. G. Factors affecting consciousness time at altitude. Part II, Air Force Technical Report No. 6009. September 1950.
8. Comfort, E. and Wilson, J. W. Some factors affecting the time of consciousness at high altitudes. Air Force Technical Report No. 5970. November 1959.
9. Hornberger, W. Pressure breathing and its physiological effect. In: German Aviation Medicine in World War II, vol. 1, p. 482. Washington, D. C., 1950. U. S. Government Printing Office.
10. Benson, O. O., Jr. The effect of decreased barometric pressure on the electrocardiogram. *J. Aviation Med.*, 11: 67, 1940.
11. Hiss, R. G., Smith, G. B. and Lamb, L. E. Pitfalls in interpreting electrocardiographic changes occurring while monitoring stress procedures. *Aerospace Med.*, 31: 9, 1960.
12. Meessen, H. Experimentelle Untersuchungen zum Collapsproblem. *Beitr. path. Anat.*, 102: 191, 1939.
13. von Diringshofen, H. Die Wirkung von Fliehkraften aud den Blutkreislauf des im Flugzeug sitzenden Menschen. *Luftfahrtmed*, 6: 152, 1942.
14. Gauer, O. Röntgenkinematographische Darstellung der Fliehkraftwirkung. *Luftfahrtmed*, 9: 109, 1944.
15. Gauer, O. and Wieckert, H. Das Elektrokardiogram des Menschen bei Fliehkraftwirkung. *Luftfahrtmed*, 9: 121, 1944.
16. Gauer, O. The physiological effects of prolonged acceleration. In: German Aviation Medicine in World War II, p. 570. Washington, D. C., 1950. Department of the Air Force.
17. Clarke, N. P., Bondurant, S. and Leverett, S. D. Human tolerance to prolonged forward and backward acceleration. *J. Aviation Med.*, 30: 1, 1959.

Pathologic Findings in the Cardiovascular Systems of Military Flying Personnel*

CAPT. R. DANIEL RIGAL, MC, USAF, MAJ. F. WARREN LOVELL, MC, USAF *and*
COL. FRANK M. TOWNSEND, MC, USAF

Washington, D. C.

SINCE the establishment of the Aerospace Pathology Branch of the Armed Forces Institute of Pathology in 1956, it has been shown that autopsies performed on the crew members in aircraft disasters can be an aid in determination of the cause and sequence of events in such accidents. Furthermore, detailed pathologic examination of the bodies of the crewmen presents an unusual opportunity to study the incidence and progression of pathologic processes in a supposedly "normal" population. Autopsy findings in military flying personnel are particularly valuable in that these men are under constant medical supervision and are considered to be clinically in excellent health at the time of their death in an aircraft accident. This is in contrast to hospital populations, on which most autopsy reports of the incidence of disease are based. The study presented here of cardiovascular disease in flying personnel shows that there is a significant incidence of moderate or marked coronary artery atherosclerosis in this group but that arteriosclerosis of other vessels has not progressed to such a degree. A parallel study made on healthy non-flying military personnel of approximately the same age group shows similar results.

Flying personnel in the United States Air Force undergo an exacting and thorough physical examination at the beginning of their flying career. This includes an electrocardiogram that is used for immediate evaluation and is then kept in a central repository for future reference. These pilots undergo an annual physical examination, which includes an electrocardiogram after the age of forty. The physical examination program is the same for aviators in the Army and Navy except that in the Army electrocardiograms are required annually regardless of age, and in the Navy there is an electrocardiogram annually after the age of forty-five if indicated. The physical standards which must be met to remain on flying status are strict.

Over 600 flying personnel are killed in military aircraft accidents annually in the United States. By regulation, autopsies are performed on these personnel. Protocols and tissues are forwarded to the Armed Forces Institute of Pathology (AFIP) for review and evaluation. While this material has the advantages enumerated, it has certain disadvantages. The high impact forces of deceleration cause marked fragmentation of many bodies. The autopsies are performed by different prosectors with a wide variety of skill and interest. The present study on the cardiovascular system was made entirely on the basis of gross descriptions, tissue sections and microscopic slides submitted by the pathologist in the field. It is realized that this imposes serious limitations on the evaluation of our data, as arteriosclerosis is a disease with irregular distribution, and in the majority of our subjects only one or two sections of coronary artery were available for review. Although we may be certain of the presence of the disease, we do not know the extent of the process in other portions of the same vessel. In subjects showing no change or minimal change we are uncertain as to the extent of the disease elsewhere in the same body. Further studies are planned in which whole hearts and aortas from aircraft accident fatalities will be sent to the AFIP for detailed gross and microscopic examination, with correlation with the electrocardiograms from the repository at the School of Aviation Medicine, USAF.

As used in this paper the term arteriosclerosis is inclusive for diseases of the arteries which pro-

* From the Aerospace Pathology Branch, Armed Forces Institute of Pathology, Washington, D. C.

TABLE 1
Incidence of Coronary Artery Atherosclerosis in Military Flying Personnel
(Aircraft Accident Fatalities)*

Age Group (yr.)	Total No.	Per Cent of Total with Coronary Sclerosis of Any Degree	Per Cent of Total with Moderate and Marked Coronary Sclerosis
20–24	66	70†	14
25–29	65	65	19
30–34	34	79	32
35–39	35	77	26
40–43	6	50	50
Age unknown	16	69	25
All ages	222	70	21

* Extracted from data of Glantz and Stembridge.[1]
† Includes one nineteen year old.

duce thickening of the arterial wall. Atherosclerosis is considered to be that type of arteriosclerosis characterized by a predominantly intimal thickening which contains both lipid and fibrous components.

Glantz and Stembridge[1] reported the incidence of coronary artery atherosclerosis in military aviators from the records at the AFIP through 1957. From 222 fatalities in which adequate material was available for review, they examined microscopically sections of the heart and coronary arteries. The age range of this group was from nineteen to forty-three; 64 per cent of the subjects were between the ages of twenty and thirty. This closely parallels the age distribution of flying personnel in the Air Force in 1956. Table 1, extracted from their data, shows that in 70 per cent of the fatalities some degree of coronary artery atherosclerosis was demonstrable and in 21 per cent it was of moderate or marked degree. Classification of the degree of sclerosis was based on the extent of luminal narrowing, as shown in Figures 1, 2 and 3. Focal thickenings of the intima that cause only slight narrowing of the lumen are classed as minimal. A more pronounced involvement of the intima causing a diminution of the lumen of from 25 to 75 per cent is considered as moderate, and a loss of lumen of more than 75 per cent is classed as marked coronary artery atherosclerosis.

By careful dissection of the coronary arteries, Enos, Holmes and Beyer[2] found gross evidence of

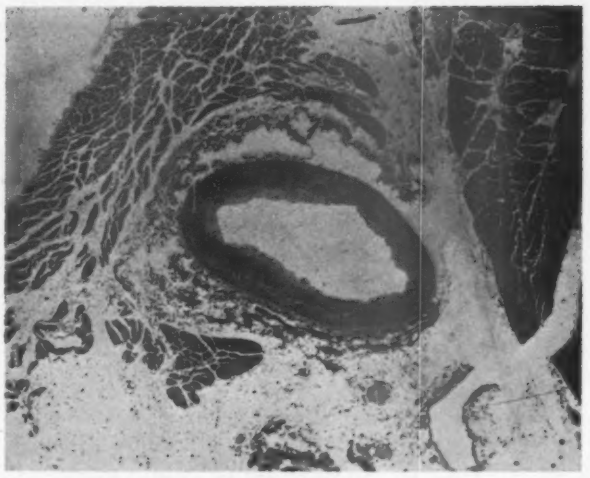


FIG. 1. Photomicrograph showing minimal coronary artery atherosclerosis. Hematoxylin and eosin stain. Original magnification × 13.

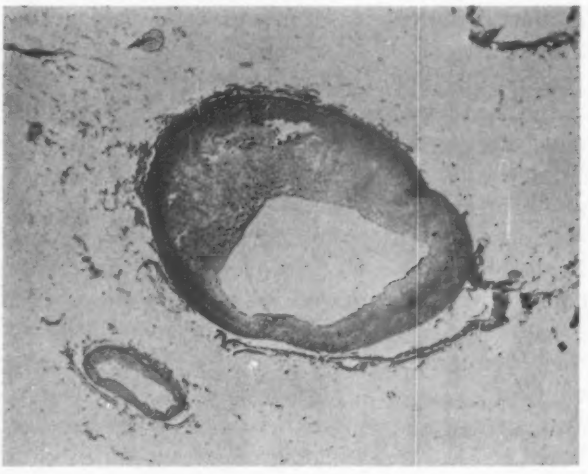


FIG. 2. Photomicrograph showing moderate coronary artery atherosclerosis. Hematoxylin and eosin stain. Original magnification × 14.

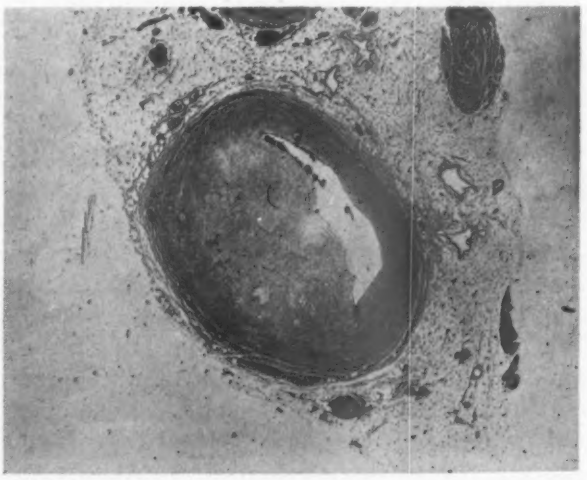


FIG. 3. Photomicrograph showing marked coronary artery atherosclerosis. Hematoxylin and eosin stain. Original magnification × 12.

TABLE II
Incidence of Coronary Artery Atherosclerosis in Non-flying Military Personnel (Accidental Deaths)

Age Group (yr.)	Total No.	Per Cent of Total with Coronary Sclerosis of Any Degree	Per Cent of Total with Moderate and Marked Coronary Sclerosis
17–19	11	45	18
20–24	90	58	13
25–29	30	73	20
30–34	18	72	28
35–39	8	62	25
40–44	6	100	33
45–47	2	100	0
Age unknown	2	50	50
All ages	167	64	18

coronary arteriosclerosis in 77.3 per cent of autopsies performed on 300 United States soldiers killed in action in Korea. This is in close agreement with the over-all incidence of 70 per cent reported by Glantz and Stembridge, even though the average age of the Korean casualties was 22.1 years as compared with the average of twenty-eight years in the flying personnel.

Material and Methods

A study was undertaken to determine whether or not there is a significant difference between the incidence and severity of coronary artery sclerosis in flying personnel and that in non-flying personnel. This was accomplished by examining records of military personnel who were not fliers but who were of the same age group as the aviators. These records were selected from the files of the Forensic Pathology Branch of the AFIP. With two exceptions, they were men on active duty with one of the military services (predominantly Army) of the United States. All these men met with accidental death, mainly the result of an automobile accident. In selecting a group that was closely comparable to the group of aircraft accident fatalities, the criteria for inclusion in the study were: (1) age less than fifty years; (2) freedom from any known significant clinical illness (specifically, illness that would have precluded flying status); (3) death the result of an accident, either instantaneously or within twenty-four hours of the time of the accident; and (4) availability of at least one adequate section of a major coronary artery.

TABLE III
Ages of Accident Fatalities by Flying Status

Age (yr.)	Flying Personnel		Non-flying Personnel	
	No. of Cases	Per Cent	No. of Cases	Per Cent
Under 20	2	1	11	7
20–24	64	31	90	54
25–29	65	32	30	18
30–34	34	16	18	11
35–39	35	17	8	5
40 and over	6	3	8	5
Total	206	100	165	100

TABLE IV
Percentages of Accident Fatalities Having Any Degree of Coronary Sclerosis, by Age

Age (yr.)	Flying Personnel		Non-flying Personnel	
	Total No.	Per Cent with Sclerosis	Total No.	Per Cent with Sclerosis
Under 20	2	50	11	45
20–24	64	70	90	58
25–29	65	65	30	73
30–34	34	79	18	72
35–39	35	77	8	62
40 and over	6	50	8	100
Total	206	70	165	64

Results

Incidence and Severity of Coronary Atherosclerosis

One hundred sixty-seven cases were found that fulfilled these criteria. The subjects ranged in age from seventeen to forty-seven years, with an average age of twenty-five. Of these, 106, or 64 per cent, had some degree of coronary artery atherosclerosis. The incidence by age groups is shown in Table II.

It should be noted that in these studies the flying personnel as a group are significantly older than the non-flying personnel as a group (Table III). This age difference, plus a lack of knowledge of the actual amount of flying done by the flying personnel, and of the duties, diet and hereditary background of all personnel, indicates that these two groups are not truly com-

TABLE V

Percentages of Accident Fatalities with Sclerosis in Which Degree Was Moderate or Marked, by Age

Age (yr.)	Flying Personnel		Non-flying Personnel	
	Total No. with Sclerosis	Per Cent with Moderate and Marked Sclerosis	Total No. with Sclerosis	Per Cent with Moderate and Marked Sclerosis
Under 20	1	0	5	40
20–24	45	20	52	23
25–29	42	29	22	27
30–34	27	41	13	38
35–39	27	33	5	40
40 and over	3	100	8	25
Total	145	30	105	28

parable for purposes of study as a single group. Thus, no definite conclusion can be drawn concerning the relation of flying to the incidence and severity of coronary artery atherosclerosis.

The incidence of coronary atherosclerosis of any degree and of moderate and marked degree in corresponding age groups of flying and non-flying military personnel is compared in Tables IV and V. The proportions of fliers and non-fliers having moderate or marked coronary sclerosis are approximately equal, regardless of age.

TABLE VI

Distribution of Arteriosclerosis in Forty-Four Cases of Moderate or Marked Coronary Artery Atherosclerosis* (Military Flying Personnel)

Site	No. with Slides Available	Incidence and Severity			
		None (%)	Minimal (%)	Moderate (%)	Marked (%)
Kidney Arcuate and interlobular arteries	42†	43	50	7	0
Aorta	27	11	85	4	0
Periadrenal arteries	26	92	8	0	0
Small arteries of pancreas	12	92	8	0	0

* Forty-four cases, with 57 per cent having moderate, and 43 per cent having marked, sclerosis.

† Nephrosclerosis of minimal degree was found in 10 per cent; none was found in the remainder.

TABLE VII

Distribution of Arteriosclerosis in Thirty Cases of Moderate or Marked Coronary Artery Atherosclerosis* (Non-flying Military Personnel)

Site	No. of Cases	Incidence and Severity			
		None (%)	Minimal (%)	Moderate (%)	Marked (%)
Kidney Arcuate and interlobular arteries	29†	59	34	7	0
Aorta	17	12	66	22	0
Periadrenal arteries	23	96	4	0	0
Small arteries of pancreas	15	93	7	0	0

* Thirty cases, with 70 per cent having moderate, and 30 per cent having marked, sclerosis.

† Nephrosclerosis of minimal degree was found in 10 per cent; none was found in the remainder.

ARTERIOSCLEROSIS IN OTHER ORGANS IN SUBJECTS WITH CORONARY ARTERY ATHEROSCLEROSIS

The interest stimulated by the papers of Enos and Glantz prompted inquiry about the degree of development of arteriosclerosis in vessels in other organs in younger people with significant coronary artery disease.

A series of records from fatalities due to aircraft accidents that showed moderate or marked coronary artery atherosclerosis, and in which there was at least one section of kidney and/or aorta available for study, were reviewed. This requirement for selecting cases is obviously a bare minimum; however, the factors peculiar to the autopsies of personnel killed in aircraft accidents, including the lack of certain tissues due to the destructive effects of impact, precluded a more extensive survey. For example, very few subjects had an adequate description or sections of the cerebral vessels available. The findings from this study are shown in Table VI. The ages of the aviators in this study ranged from twenty to forty-nine years, with an average age of twenty-eight years.

A similar study was carried out on subjects with moderate or marked coronary sclerosis among non-flying military personnel. The distribution and incidence of arteriosclerosis in other organs as shown in Table VII are nearly the same as those noted in the corresponding group of fliers.

Aorta: In approximately half the records in which slides of the aorta were present, there were also gross descriptions of the aorta. These de-

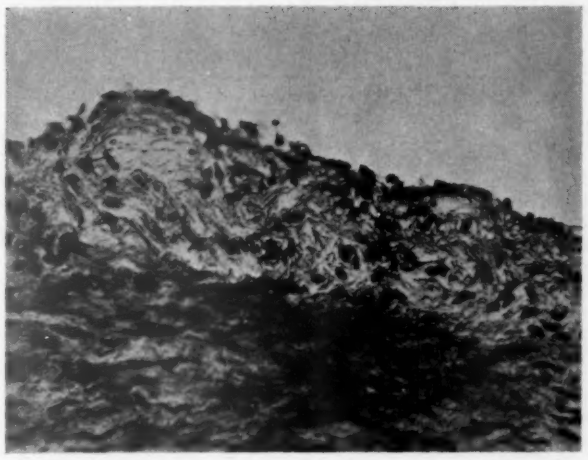


FIG. 4. Photomicrograph showing minimal atherosclerosis of coronary artery illustrating predominantly fibrous character. Hematoxylin and eosin stain. Original magnification × 305.

FIG. 5. Photomicrograph showing minimal atherosclerosis of aorta with accumulation of lipophages and increase of metachromatic intimal ground substance. Hematoxylin and eosin stain. Original magnification × 220.

scriptions either agreed with the microscopic findings or stated that there was no atherosclerosis, when microscopic study showed a minimal degree. In general, the picture of the minimal lesion in the aorta is one of intimal thickening due to accumulation of lipid laden macrophages and an increase of metachromatic intimal ground substance. In contrast, the minimal thickening of the intima of the coronary arteries appears to be predominantly fibrous in nature (Figs. 4 and 5).

Kidneys: Sclerosis of renal arterioles was occasionally noted. This finding was not included in Tables VI and VII, however, because the degree of involvement was so minimal that consistent estimates of incidence could not be made.

Relation of Coronary and Generalized Arteriosclerosis: As early as 1896 Dock[3] stated that severe coronary artery disease could be found in rare cases in the absence of significant atherosclerosis in other arteries. However, Duff[4] stated that atherosclerosis of the coronary arteries generally develops later and is less severe than that in the aorta, but that it is not uncommon to see severe coronary artery disease in the presence of relatively slight atherosclerosis of the aorta. In a series of autopsies performed on men under forty years of age who died from the effects of coronary artery disease, Yater et al.[5] found that the amount of atherosclerosis of the aorta was slight or moderate in comparison to the degree of sclerosis in the coronary arteries. As a result of our study, we are in agreement with Yater that coronary artery atherosclerosis in younger persons may be an independent process and not necessarily a part of generalized arteriosclerosis.

CORRELATION OF CORONARY ARTERY ATHEROSCLEROSIS WITH THE CAUSE OF AIRCRAFT ACCIDENTS

The correlation of the finding of marked coronary artery disease with other factors in determining the cause of an accident is sometimes a difficult problem. Unfortunately, the pathologic-anatomic changes of sudden death are often not clear-cut, and many physicians do not realize that in up to 75 per cent of the cases of sudden death clinically attributed to coronary occlusion, there is no demonstrable thrombus but only a marked narrowing due to atherosclerosis.[6] In a few instances there may be an old thrombus or a hemorrhage into an intimal plaque.

The following case reports illustrate the type of problems encountered.

CASE 1. A thirty-four year old pilot (AFIP Acc. No. 870232) was ejected at low altitude after the wing

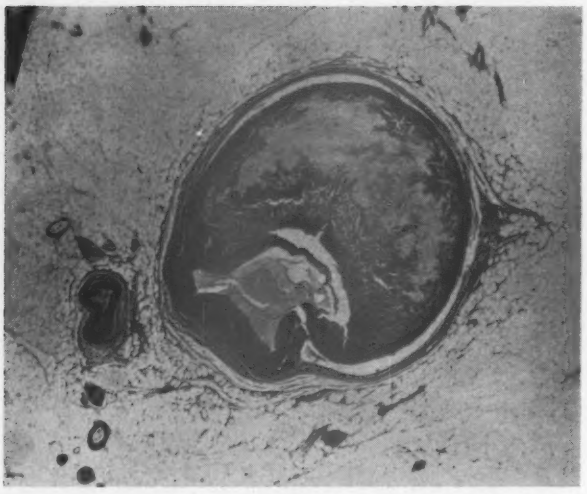


FIG. 6. Case 2. Photomicrograph of coronary artery with marked atherosclerosis. Hematoxylin and eosin stain. Original magnification × 20.

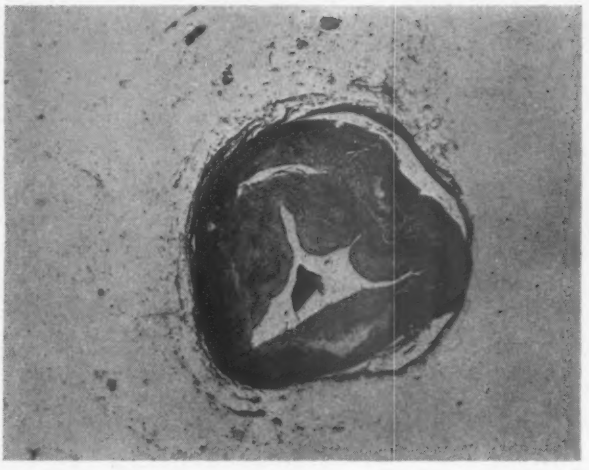


FIG. 8. Case 3. Photomicrograph of coronary artery showing marked atherosclerosis with necrotic, vascularized atheroma. Hematoxylin and eosin stain. Original magnification × 14.

of his F9F jet aircraft folded at approximately 1,400 feet. He died instantly as a result of abrupt deceleration on impact with the ground.

At autopsy, severe coronary artery atherosclerosis was found. There was no evidence of infarction or fibrosis of the myocardium. It is clear in this instance that the coronary artery disease was unrelated to the accident. However, had the circumstances of the accident not been known, the question of physiologic incapacitation of the pilot secondary to sudden coronary insufficiency could well have been raised.

CASE 2. A twenty-six year old pilot (AFIP Acc. No. 914057), flying an FJ-4B aircraft, was in a flight of two aircraft entering an airfield landing pattern. The tower instructed them to turn on their lights. Following this the pilot allowed his plane to get below the landing pattern altitude by some undetermined distance. He called in at this time stating "turning base, gear down, for a touch-and-go landing," which indicated that he was making a turn at right angles to the runway and was ready to land. His plane was then observed to enter a descending turn toward the runway and shortly thereafter to fall sharply, strike the ground, and explode.

At autopsy, in addition to extensive traumatic injuries, severe atherosclerosis of the coronary arteries and focal fibrosis of the myocardium were found (Figs. 6 and 7). In such a case, incapacitation or sudden death as a result of severe cardiac arrhythmia secondary to coronary insufficiency would certainly be likely. Here, however, spatial disorientation, perhaps occurring at the moment when landing lights were turned on, must also be considered a strong possibility.

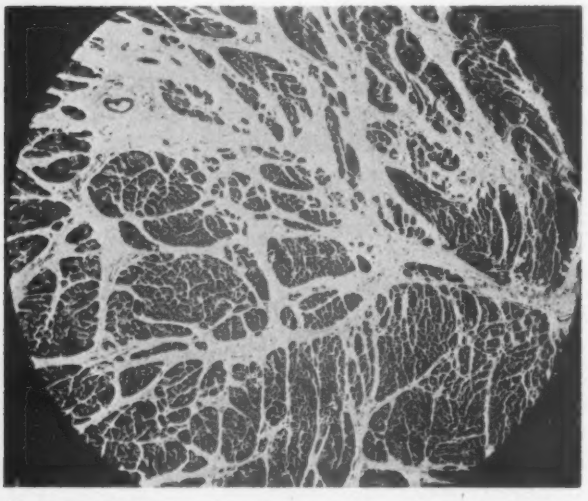


FIG. 7. Case 2. Photomicrograph of heart showing fibrosis of myocardium. Hematoxylin and eosin stain. Original magnification × 35.

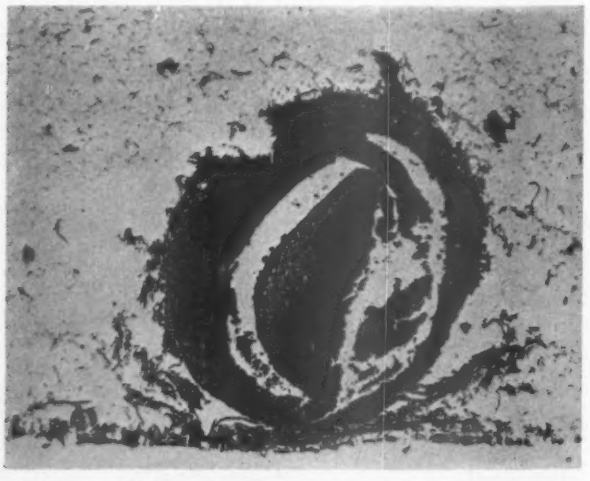


FIG. 9. Case 3. Photomicrograph of coronary artery showing medial hemorrhage. Hematoxylin and eosin stain. Original magnification × 26.

CASE 3. A Navy instructor pilot (AFIP Acc. No. 912765) was flying a T28 aircraft on a carrier exercise in marginal weather. There was evidently confusion on the radio, during which time the aircraft struck the water with high impact.

At autopsy, the pilot was found to have severe coronary artery atherosclerosis with hemorrhage into an atheromatous plaque. Such an episode could have caused sudden incapacitation, which at low altitude and in confusing flying conditions could result in loss of control of the plane and collision with the water. While this is the most probable explanation for the accident, other contributory factors such as spatial disorientation cannot be entirely ruled out, and the hemorrhage conceivably could have been precipitated by the trauma of impact (Figs. 8 and 9).

CASE 4. In response to an alert, a thirty year old pilot (AFIP Acc. No. 900049) ran to his aircraft and started the engine. After beginning to taxi, he was seen to stop, then slump forward over the controls. His aircraft rolled forward until it struck another aircraft and stopped. One of the line crew rushed to the aircraft, jettisoned the canopy and lifted the pilot from the cockpit. The pilot was pronounced dead on arrival at the dispensary.

At autopsy, the heart was found to be enlarged, weighing 450 gm. The circumflex branch of the left coronary artery was considerably narrowed, and microscopic examination showed a florid atherosclerosis with marked lymphocytic infiltration into the atheroma and surrounding media. There was no infarction of the myocardium.

The finding of severe coronary atherosclerosis together with a knowledge of the details of the accident indicate that it was highly probable that the pilot's death and the subsequent accident resulted from the effects of acute coronary insufficiency.

SUMMARY AND CONCLUSIONS

In a group of supposedly healthy young fliers, there is a significant percentage who have moderate or marked atherosclerosis of the coronary arteries. However, in these pilots there is very little arteriosclerosis in the aorta, renal arcuate arteries, and small arteries of the periadrenal fat and the pancreas. The same observations are essentially true of a similar group of non-flying military personnel. This suggests that in young men free of clinical evidence of disease, coronary artery atherosclerosis may develop at a more rapid rate than in vessels of other organs. Fliers and non-fliers in the present study were not basically comparable because of age and other differences. However, the incidence of moderate and marked coronary artery sclerosis was found to be approximately equal in both groups, regardless of age.

In implicating marked coronary artery disease as a causative factor in an otherwise unexplained aircraft accident, extreme caution must be used. The finding of severe narrowing of the lumen of the coronary arteries must be considered in the light of information gained from the investigation of mechanical factors and from reports of the details of the accident.

REFERENCES

1. GLANTZ, W. M. and STEMBRIDGE, V. A. Coronary artery atherosclerosis as a factor in aircraft accident fatalities. *J. Aviation Med.*, 30: 75, 1959.
2. ENOS, W. F., HOLMES, R. H. and BEYER, J. Coronary disease among United States soldiers killed in action in Korea. *J. A. M. A.*, 152: 1090, 1953.
3. DOCK, G. Notes on the Coronary Arteries. Ann Arbor, Michigan, 1896. The Inland Press. Reproduced in MAJOR, R. H. Classic Descriptions of Disease, p. 431. Springfield, Ill., 1955. Charles C Thomas.
4. DUFF, G. L. and MCMILLAN, G. C. Pathology of atherosclerosis. *Am. J. Med.*, 36: 92, 1951.
5. YATER, W. M., TRAUM, A. H., BROWN, W. G., FITZGERALD, R. P., GEISLER, M. A. and WILCOX, B. B. Coronary artery disease in men eighteen to thirty-nine years of age. *Am. Heart J.*, 36: 113, 1948.
6. GONZALES, T. A., VANCE, M., HELPERN, M. and UMBERGER, C. Legal Medicine, Pathology and Toxicology, p. 113. New York, 1954. Appleton-Century-Crofts, Inc.

Cardiovascular System of the Aging Pilot*

BRIG. GEN. OTIS B. SCHREUDER, MC, USAF (RET.) *and* JOSEPH G. CONSTANTINO, M.D.
New York, New York

ACCORDING to a recent editorial,[1] "One of the chief difficulties in studying the aging process is that no sure way is known at present to separate physiological sclerosis (the age-conditioned consolidation of tissues) from arteriosclerosis, to which it is not related histologically or pathogenetically. The concept that you are as old as your arteries does not get to the root of the matter, because aging is a process that can be recognized in plants and in animals that do not have arteries but in which a period of growth is followed by cessation of growth, decline and death. Arteriosclerosis is also unevenly distributed in the body; thus, the physiological process is masked by the pathological."

In approximately 25 per cent of men over forty years of age and 40 per cent of men over fifty years of age, there is some degree of elevation of blood pressure based on a normal systolic pressure of below 150 mm. Hg.[2] In this connection statistics from insurance companies show that there is a definite relation between high systolic and diastolic blood pressures and life expectancy. These statistics also show a relation between overweight and the probability that one of the degenerative diseases will develop, particularly hypertension or diabetes with a resulting decrease in longevity.

Aging is a complicated process which begins with birth and ends with death, although usually one thinks of the aging process as beginning in maturity. This is true of the aging process of the cardiovascular system as well as the other systems of the body.

CARDIOVASCULAR COMPLICATIONS OF AGING

With increasing age there may be slowly progressive changes in the cardiovascular system such as a tendency for the heart to get proportionately larger, which, however, does not mean that it has increased in functional capability. There also may be deposition of cholesterol or calcium deposits on the valves of the heart. The systolic pressure invariably increases after the age of forty years and with increased age, the pulse rate may not respond as well after exertion and stress. The elasticity of the blood vessels usually decreases.

Although frequently there are no significant electrocardiographic changes, the following changes may occur: low voltage and slurring of QRS with a tendency to increased duration, a decrease in the amplitude of the P wave, and T wave changes. There is also an increased frequency of functional arrhythmias.

Of particular interest is the occurrence of coronary artery disease, the incidence of which increases with age but which nevertheless often occurs at a relatively young age. The majority of workers now consider this as a disease rather than as a part of the normal aging process. The occurrence of coronary artery disease is of utmost importance in the airline pilot because of the possibility of sudden incapacitation.

In the older age group, deaths from cardiovascular-renal disease exceed all other causes. In the past twenty-five years the population of the United States has doubled, and the population of older persons has quadrupled. The major threat to these senior citizens is disease of the blood vessels.[3] In 1900 diseases of the heart and blood vessels were responsible for the death of two of ten persons, whereas in 1955, over five of every ten in the United States died from these causes. A study of the cardiovascular-renal deaths in 1955[4] revealed that 48.8 per cent of the people died of arteriosclerotic heart disease, including coronary artery disease, and 20.9 per cent of cerebral vascular lesions. From these studies it appears that the underlying pathologic finding in most of the deaths from cardiovascular disease is atherosclerosis. Approximately 40 per cent of men over forty years of age in the United States have significant atherosclerosis of their coronary vessels.[4]

* From the Overseas Division, Pan American World Airways, Inc., New York, New York.

Cardiovascular Disease in Airline Pilots

Although the incidence of cardiovascular-renal disease is relatively high in most walks of life beginning with middle age, it has been our observation that the incidence is lower among airplane pilots. For example, in Pan American World Airways from January 1958 to May 1959 there have been thirty-seven pilots who have become unfit for flying duties because of some disease process (not including injuries). Of the group twenty have died and seventeen are living. In eleven instances, incapacitation was due to neurologic and psychiatric conditions and in eight it was due to disease of the cardiovascular system. The cardiovascular conditions included six cases of coronary occlusion with myocardial infarction; in four of these the pilots are living.[5]

In a study of the medical records of 150 active senior pilots over forty years of age, cardiovascular defects as well as other defects occurred rather infrequently. The average age of these pilots was 44.1 years with only fifteen pilots in the age group between fifty-one and sixty years. There were five (3.3 per cent) who exhibited potential arterial hypertension; thirteen (8.7 per cent) who could be considered to be overweight according to life insurance standards and two (1.3 per cent) who had borderline cardiac hypertrophy. In eleven instances (7.3 per cent) there were minor electrocardiographic changes. All pilots exhibiting these minor cardiovascular defects were entirely without symptoms. It is interesting to note that of the total number of pilots in the Overseas Division of Pan American World Airways, 33 per cent are in the age group from forty to sixty years.

The lower incidence of cardiovascular-renal disease as well as the lower incidence of the other degenerative diseases is in this group partially due to the rigid physical examination given prior to acceptance. The pilot is qualified medically on his original examination on the basis not only of his present physical condition, but also on his potential physical condition twenty to thirty years hence. A rigid appraisal of the cardiovascular system is mandatory during the original examination. For example, in 1955 in the examination of 186 applicants for the position of co-pilot, fifty were medically disqualified, a rejection rate of 26.8 per cent. Among the fifty rejectees there were 124 physical defects; of these twenty-six were visual and ocular defects; twenty were chronic, early or obviously potential cardiovascular defects; and nineteen were neuropsychiatric conditions. In the original examination of the applicant a routine twelve-lead electrocardiogram is taken to aid in ruling out cardiovascular disease. If accepted, this original electrocardiogram serves as a baseline record for future reference.

The primary mission of the medical department of an airline is the preservation of health of the employees and the safety, comfort and welfare of the passengers. In the interest of flight safety particular attention is given to the operational members of the aircrew. The periodic physical examination is one of the means of maintaining the pilot in good health, its objective being to detect any disease process in its earliest stage so that corrective action can be taken. With reference to the cardiovascular system a routine twelve-lead electrocardiogram is taken yearly after the age of thirty-five years and annual tests of postprandial blood sugar and blood cholesterol are made after the age of forty years.

Illustrative Cases

The following case reports are representative of some of the cardiovascular conditions found and the action taken.

Case 1. A thirty-six year old pilot was off flight duty for five weeks. He had been hospitalized for two and a half weeks, supposedly for an acute nonspecific pericarditis, and applied for reinstatement to flight status. Physical examination, including an electrocardiogram, revealed that the pilot was still in ill health and a diagnosis of a recent anteroseptal infarction was made. Of particular interest was the family history which revealed that his father died from a "heart attack" and that an older brother had recently suffered a coronary occlusion. Previous physical examinations, including electrocardiograms, did not reveal evidence of coronary sclerosis. He was obviously not qualified for flight duties and was given a ground assignment which he performed satisfactorily until a fatal coronary occlusion with infarction occurred four years and three months later.

Comment: This case is of particular interest because it substantiates the opinion, currently held in aviation medicine circles, that a pilot who has had a definite coronary occlusion with myocardial infarction should be permanently disqualified from duties as a pilot.

Case 2. A twenty-six year old flight engineer had served four years in military service in a similar capacity without difficulty and two years in commer-

cial aviation when a diagnosis of aortic insufficiency was made on the basis of clinical findings including a characteristic murmur, high pulse pressure and a Corrigan pulse. The electrocardiogram was normal. The patient was asymptomatic and his cardiac reserve was excellent. A résumé of the history revealed questionable "growing pains" between the ages of six to eight years but a definite diagnosis of rheumatic fever had not been made. It was our belief that the aortic valve lesion had been present probably since the age of twelve years and was of rheumatic origin. For administrative reasons he was placed on furlough status and was advised that in the interest of his future health he should seek employment on a ground status.

Comment: This case is interesting in that it points out the difficulty in early diagnosis of valvular heart disease in the absence of definite history of rheumatic fever and particularly when a young person has successfully completed a tour of duty with the Armed Forces.

Case 3. A thirty-three year old pilot had a normal electrocardiographic tracing during an annual physical examination. He continued to enjoy good health and the interim medical history was noncontributory. Two years later, at the age of thirty-five, a left bundle branch block was discovered during a routine annual physical examination. The pilot was completely asymptomatic and showed no disease or roentgenographic evidence of heart disease or of diminished cardiac or coronary reserve. It was impossible to state the cause of the bundle branch block. He was cleared for flight duties and has continued to be asymptomatic. Periodic electrocardiograms still reveal the presence of a left bundle branch block two and a half years later but he continues to be asymptomatic and in good health.

Case 4. An applicant for the position of co-pilot, age twenty-seven years, was employed after a thorough physical examination including an electrocardiogram which was normal. He was called to active reserve duty with the Armed Forces as a pilot for one year. The interval history was excellent with a noncontributory medical history. On return from military leave of absence at the age of thirty-one years, physical examination revealed electrocardiographic abnormalities of both atrioventricular and intraventricular conduction without physical, functional or roentgenographic evidence of heart disease. The fact that a normal electrocardiogram had been recorded only four years ago strongly suggested that the abnormalities had developed on the basis of organic disease. However, after a thorough study, including a consultation with a competent cardiologist, he was qualified for flight status. He has had yearly physical examinations including electrocardiograms which have revealed no change. He is now thirty-six years of age and in good health.

Comment: Whether or not further cardiovascular disease will develop in the future is still problematic. The atrioventricular block is of more importance than the intraventricular block and if the former is organic in nature it may at some time become more severe and lead to higher degrees of atrioventricular block. This case also illustrates the value of annual electrocardiograms as part of a physical examination, whether in commercial or military aviation.

Criteria of Early Cardiovascular Disease

Frequently one finds that a physical examination does not reveal sufficient significant changes to warrant a diagnosis of early cardiovascular disease; however, it is important that the examiner be observant for changes even though they may seem insignificant at the time. The following criteria are helpful in arousing suspicion of early cardiovascular disease: (1) patient looks older than stated age; (2) premature graying of the hair; (3) history of early alopecia; (4) occurrence of xanthomas; (5) family history of cardiovascular disease particularly in the early age group between twenty and forty years; (6) obesity; (7) tortuosity of the retinal and peripheral vessels; (8) labile blood pressure and pulse; and (9) increase in heart size as determined by physical examination and roentgenogram.

It has been found that there are certain diagnostic measures which are of aid in the diagnosis of early cardiovascular disease. Among these diagnostic measures are: (1) an electrocardiogram; (2) a ballistocardiogram; (3) roentgenographic studies of the heart and great vessels; (4) a hemogram profile; (5) blood lipoproteins; (6) blood cholesterol; and (7) thyroid function studies such as basal metabolism and protein-bound iodine. One must realize, of course, that although all of the aforementioned tests may be well within normal limits the patient may still have cardiovascular disease, particularly involvement of the coronary arteries.

Preventive Measures

Although there is a serious concern that early cardiovascular disease may curtail the pilot's active flying career, it does not appear that this will necessarily occur. It has been our observation that our older pilots are in a relatively good state of health, not only from the cardiovascular standpoint but also when the other

systems of the body are considered. It is believed that this is also true of other airlines which have well organized medical departments. The reasons for this are: (1) airplane pilots are a highly selective group; (2) the periodic physical examination has disclosed some medical conditions which have been corrected; (3) the physical examinations have made the majority of pilots conscious of their health; (4) some pilots have been forced to discontinue their pilot duties because of personal or technical reasons or because they have incurred a serious illness or injury other than cardiovascular disease; and (5) from an economic standpoint the pilot knows that his job depends upon his continued good health and good physical condition. The major concern, of course, is still the problem of acute coronary disease with infarction because of sudden incapacitation as far as flying is concerned.

Whether or not preventive measures can delay changes in the cardiovascular system is problematic. However, it is our firm belief that certain measures improve the pilot physically and mentally and indirectly increase his proficiency. As a result of this thinking, a program of health education or counseling has long been in order in connection with the periodic physical examination. It is quite possible that the following measures might be factors in slowing the aging process of not only the cardiovascular but also the other systems of the body: (1) proper amount of physical exercise; (2) mental activity with a proper outlook on life; (3) moderation in food intake, drinking and smoking; (4) proper amount of sleep daily; and (5) avoidance of obesity. Specific measures, such as low cholesterol diets and glandular therapy, are still in the experimental stage and cannot be universally recommended at this time.

Although enormous advances are being made in medicine, a great deal remains to be done in the field of aging, particularly in the field of early detection of cardiovascular disease. It is hoped that the intensive research, which is being performed today, will give us new and more specific diagnostic measures so that preventive steps can be taken to improve the health and life expectancy of the aging pilot.

Summary

With the increasing average age of the airline pilot, the pathologic changes which occur in the cardiovascular system with the aging process are becoming more and more important. Statistical studies reveal that deaths from cardiovascular-renal disease exceed all other causes in the older age groups. It has been observed, however, that the incidence of this disease among pilots from middle age on is lower than in most other walks of life, largely due to the fact that they are a highly selective group. A rigid appraisal of the cardiovascular system during the original preplacement examination is considered mandatory.

Four representative cases are presented as illustrative of some of the existing problems. The criteria or changes which should arouse suspicion of early cardiovascular disease and the diagnostic measures which are of aid in establishing this condition are outlined. Preventive measures which may delay changes in the cardiovascular system are also presented.

References

1. Editorial: Aging. *J.A.M.A.*, 162: 208, 1956.
2. Stieglitz, E. J. Geriatric Medicine, p. 462. Philadelphia, 1949. W. B. Saunders Co.
3. Bortz, E. L. The challenge of longer life. *The Pharos, Alpha Omega Alpha Journal*, 18:5, 1955.
4. Hilleboe, H. E. and Larimore, G. W. Preventive Medicine, pp. 532–533. Philadelphia, 1959. W. B. Saunders Co.
5. Statistical data, Pan American World Airways Medical Committee, 1959.

The Problem of Elevated Blood Pressure or Hypertension in the Pilot*

LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

DETERMINATION of whether a person simply has elevated blood pressure or hypertensive disease is a difficult problem even in ordinary clinical practice. It is magnified considerably when applied to the aeromedical situation. At least in unrestricted flying categories requiring that the subject be capable of primary control of high performance aircraft, the concept that pilots should not be receiving any form of significant medication has considerable merit. Operating such aircraft requires maximum efficiency of reflex action, mental alertness and maintenance of the integrity of cardiovascular dynamics. It is obvious that sedatives for the treatment of hypertension do not permit flying safety in this situation and that sympathetic blocking agents which remove control of peripheral resistance remove protection against increased g force. It must be assumed, then, that the retention of a person in such an unrestricted flying category implies that antihypertensive therapy cannot be given. If it is decided that a patient needs antihypertensive therapy, then his flying career must be sacrificed.

In dealing with the young flying population, we sometimes see examples of labile blood pressure. Is this a manifestation of future hypertensive disease? How accurate are the concepts of vascular hyperreactor, normal reactor and hyporeactor for predicting the development of future vascular disease? Are we justified in assuming that a young man with intermittent elevation of blood pressure is going to be a poor risk to enter an expensive training program costing in many instances over a million dollars, or should we eliminate these persons at the onset of their career? Are they, because of their interest, anxiety and perhaps hyperreactive characteristics, the more successful candidates essential to a unit that will carry out combat missions? The satisfactory answer to this question needs to be known in matters pertaining to selection alone. Finally, when do we decide that an elevated blood pressure is truly abnormal? Can we really define blood pressure levels as normal or abnormal? These points are in many ways of particular importance to those concerned with industrial medicine, life insurance and the aeromedical and military fields. One might well ignore a moderately elevated blood pressure with no symptomatology in civilian life, but its significance in terms of selection and prognosis is more important to the groups mentioned.

METHOD OF STUDY

Recognizing that opinions differed greatly on many facets of this problem, we attempted to obtain some expression of the general opinion of authorities in the field. A questionnaire was sent to leading authorities throughout the world. The letter accompanying the questionnaire explained that it was important for the reasons discussed and it was understood by the experts supplying answers to the questionnaire that it was for our use in the flying population. This alerted them to the fact that we were dealing with younger people, not the usual clinical situation. Undoubtedly this colored the type of answers received. The questions themselves were directed strictly to the medical aspects of hypertension. This was thought to be prudent, as many authorities in hypertension have relatively little or no knowledge concerning aeromedical problems although they may be experts in the intricacies of hypertension.

The answers provide an interesting cross section of thinking on the problems related to hypertension and will undoubtedly provide much for discussion. Answers were returned by twenty-seven of the thirty authorities queried. The twenty-seven replying to the questionnaire were Drs. Byron Pollock, E. Grey

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

TABLE I
Authorities' Opinions of the Upper Limit of Normal for Systolic Blood Pressure

Pressure (mm. Hg)	No. of Opinions
Below Age of 40 Years	
130	1
138	1
139	1
140	16
150	5
160	1
Above Age of 40 Years	
139	1
140	8
150	10
155	1
160	2
180	2

TABLE II
Authorities' Opinions of the Upper Limit of Normal for Diastolic Blood Pressure

Pressure (mm. Hg)	No. of Opinions
Below Age of 40 Years	
85	5
88	1
89	1
90	18
100	1
Above Age of 40 Years	
85	1
89	1
90	19
95	3
100	1
110	1

Dimond, R. Bruce Logue, S. W. Hoobler, James Warren, George A. Perera, Carlton Chapman, Robert Wilkins, Edward Fries, George W. Manning, Tinsley Harrison, Howard Lewis, Robert Bruce, Charles Kossmann, Eugene Stead, Robert P. Grant, Ashton Graybiel, John Moyer, Samuel A. Levine, Paul D. White, Howard Burchell, Irvine Page, Lewis Dexter, Arthur Fishberg, Henry Schroeder, Harry Ungerleider and John Pickering.

RESULTS OF QUESTIONNAIRE

Upper Limit of Normal for Systolic Pressure: The first question was intended to determine what most authorities considered the upper limit of normal for the systolic blood pressure in persons below the age of forty years. Twenty-five doctors replied to this question (Table I). Of the twenty-five, sixteen thought that 140 mm. Hg was the upper limit of normal; thus the median and the mode was 140 mm. Hg and the mean was 142 mm. Hg. The second point was what level of systolic blood pressure represented the upper limit of normal for persons past the age of forty years (Table I). Of twenty-four who replied to this question, ten believed that 150 mm. Hg was the upper limit of normal. The median and the mean was 150 mm. Hg.

Upper Limit of Normal for Diastolic Pressure: The third point concerned the upper limit of normal for the diastolic blood pressure below the age of forty years. It was specifically stated on the questionnaire that the diastolic pressure referred to the disappearance of sound. Of twenty-seven replies received there were twenty-six satisfactory answers (Table II). Eighteen authorities believed that the upper limit of normal for the diastolic pressure below the age of forty years was 90 mm. Hg. The median and the mode was 90 mm. Hg and the mean was 89 mm. Hg.

The fourth point to be established was the upper limit of normal for the diastolic blood pressure in persons forty years of age or over. Of twenty-six who replied to this question, nineteen believed that 90 mm. Hg was the upper limit of normal for this age group (Table II). Both the median and mode for the replies indicated that 90 mm. Hg was the upper limit of normal; the mean was 92 mm. Hg. In summary, then, the group opinion seemed to indicate that the upper limit of normal for blood pressure levels below the age of forty years was 140/90 mm. Hg and above the age of forty, 150/90 mm. Hg.

Intermittent Blood Pressure Elevation: The fifth point to establish was the significance of intermittent elevated blood pressure. This question was deliberately framed in such a way that normal blood pressure determinations were only occasional and read, "What diagnosis or opinion would you give in an individual who has blood pressure determinations above the

TABLE III
Authorities' Opinions Regarding What Level of Blood Pressure is an Indication for Therapy

Pressure (mm. Hg)	No. of Opinions
Systolic	
None for systolic	6
150	1
160	2
170	1
180	5
200	1
Diastolic	
90–95	1
100	5
110	5
120	1
120, 130 or 140	1

level of your normal values and has occasional determinations within your prescribed normal limits?" The replies were somewhat varied. Of twenty-one answers that could be fairly well classified, thirteen implied that the findings in such a person were significant. They indicated this by use of such terms as prehypertension, hypertension or potential hypertension. Another seven authorities believed that such subjects were normal or classified them as vascular hyperreactors. One authority chose the term "labile high blood pressure" but it was not clear what significance he attached to this particular term. It was of interest that only five authorities actually used the unqualified term hypertension in describing persons with this finding alone.

Level of Blood Pressure and Indication for Treatment: The sixth point to be established was in reference to treatment and because of a clerical error the value of this question was lost, in part, to the survey. The question read: "Assuming no other significant findings (normal heart size, normal Master exercise tolerance test, normal renal function and asymptomatic), at what level of systolic blood pressure would you institute treatment, if at all?" Of sixteen replies to this question, six indicated that no treatment would be indicated and ten would institute treatment at various levels of systolic elevation (Table III). Five more authorities stated that if the systolic pressure were 180 mm. Hg or more, they would institute treatment. This figure represented the median opinion of the group. The mode was also 180 mm. Hg and the mean was 174 mm. Hg.

Fortunately, thirteen authorities also indicated their attitude concerning the treatment of diastolic pressure (Table III). One authority would institute therapy of diastolic blood pressure levels as low as 90 to 95 mm. Hg; another indicated that in many instances he would not institute therapy unless the diastolic pressure was as high as 140 mm. Hg. For the level of diastolic pressure at which treatment should be instituted, the mode for the replies was 100 to 110 mm. Hg, the median 110 mm. Hg and the mean 107 mm. Hg. Apparently only one authority believed that treatment at diastolic levels below 100 mm. Hg as a sole finding was indicated.

Effect of Treatment on Prognosis: The next question inquired, "Do you have any factual information that control of blood pressure to normotensive levels in the individual with the finding of blood pressure elevation alone actually improves the prognosis?" Of twenty-four replies to this question, nineteen said "no" and 5 said "yes." In this group of five may be included several who interpreted the question to include hypertensive crisis. The following comments were volunteered in response to this question: "There is no question in my mind that adequate treatment may sometimes cause reversal of hypertension to the point that drugs are no longer necessary (seen thirty times—four in the malignant)." Another authority replied, "No, neither has anyone else." A third reply was, "Yes, in the malignant phase and in that only." The responses would indicate that there are few authorities who, at the present time, believe that therapy for uncomplicated essential hypertension actually improves the prognosis.

Elevated Blood Pressure and Restriction of Physical Activity: The next question was intended to learn what the authorities thought about the limitation of activity in subjects with elevated blood pressure as the only finding. The question read: "Do you feel that any restriction should be placed on physical activity with elevated blood pressure as the only finding in individuals below the age of 40? In individuals above the age of 40?" Of those persons over forty years of age, twenty authorities thought that no restriction in activity was

indicated for elevation of blood pressure alone. One authority said slight restriction was indicated and two believed that restriction was indicated. For persons below the age of forty years with elevated blood pressure, twenty-one authorities said that no restriction was indicated, two believed slight restriction was in order and one thought that restriction was indicated.

Vascular Changes in Fundi: Since there is considerable controversy concerning the significance of vascular findings of the fundi as related to establishing the diagnosis of hypertension or prognosis, questions were directed toward this point. One question asked, "Would you give medication or treatment or limit activity in any way in the individual with grade 1 or 2 Keith-Wagener changes in the fundi and with transitory blood pressure elevations above your normal value but with frequent normal levels?" Of twenty-five authorities, eighteen replied "no"; seven said "yes."

The question was then asked "Do you think grade 1 or 2 Keith-Wagener changes of fundi may be transitory in the same sense that one's blood pressure is elevated as a manifestation of vascular hyper-reactivity?" Of twenty-one authorities answering this question, fourteen replied "yes"; seven said "no." An interesting point made by one of the authorities which bears repetition was, "I think these changes are valueless. Observer error has been carefully studied and it is enormous." Several authorities expressed doubt concerning the significance of the Keith-Wagener classification. One authority said it depended on who observed them. Others indicated that very often grade 1 and 2 changes were in reality arteriosclerotic rather than hypertensive changes. Nevertheless, the total group of answers would seem to indicate that the usual concept of grade 1 and 2 Keith-Wagener changes is limited in its ability to substantiate the diagnosis of hypertension.

Comments

Such a survey is definitely limited in the range of its applicability. Nevertheless, it does bring forth certain ideas which are applicable to those engaged in active flying careers. It must be stated that in all likelihood different answers would have been received from the same authorities were they dealing with older populations. It must also be recognized that these replies were based on the assumption that blood pressure elevations were the only discernible manifestation of disorder. It may be said that the majority of opinion holds that persistent blood pressure determinations above 140/90 mm. Hg in subjects below the age of forty years are significant and that persistent blood pressure elevations above 150/90 mm. Hg in persons above the age of forty years are likewise significant. The replies indicate that when blood pressure elevation is the only finding and when such elevations are not persistent, most authorities would be reluctant to make a diagnosis of hypertension. The third and perhaps the most important consideration in this survey is that most authorities would be reluctant to begin treatment when elevated blood pressure was the only finding unless the blood pressure levels were approximately 170/110–100 mm. Hg. Finally, the majority of authorities had no real faith that modern antihypertensive therapy really improved the prognosis in persons in whom the only finding was persistent elevation of blood pressure. Therefore, it would seem logical that, in the pilot without evidence of vascular complication or evidence of any other form of complication of elevated blood pressure, it would be acceptable for him to continue his flying career and not institute therapy until the diastolic pressure was persistently elevated above 100 mm. Hg. One need not think that any great compromise in health or prognosis has been made by pursuing this course of action.

Of course, the usual hygienic control measures, such as weight reduction and maintenance of adequate physical activity, are indicated. It is hoped that these measures would, to some extent, help prevent some of the common arteriosclerotic complications of hypertension. In individual instances it might be acceptable to continue a pilot in an active flying career without medication even with diastolic blood pressure elevations up to 110 mm. Hg. Beyond this point, more serious consideration concerning the advisability of therapy and cessation of unrestricted flying must be given on an individual basis.

As our knowledge improves concerning the over-all problem of hypertension, perhaps a true answer can be given as to the significance of transitory elevation of blood pressure in the so-called vascular hyperreactor and the influence on prognosis of more recent forms of antihypertensive therapy. Perhaps when we can better control the arteriosclerotic complica-

tions attendant to hypertension, the approach to the problem will require revision. Until such time, the approach outlined herein seems logical for the pilot in the unrestricted flying category.

Summary

An opinion survey of twenty-seven authorities relative to the normal level of blood pressure has been carried out. Most replies indicated that 140/90 mm. Hg was the accepted upper limit of normal for blood pressure in persons under forty years of age and that 150/90 mm. Hg was the accepted upper limit of normal for persons past the age of forty years.

Opinions were expressed and are reported relative to the significance of intermittent blood pressure elevations, the level of blood pressure which should be an indication for therapy when blood pressure elevation was the only finding and information, if any, relative to improvement in prognosis resulting from therapy.

Comments relative to the problem of hypertension and therapy as related to flying are included.

The Prognostic Implications of the Electrocardiogram*

HARRY E. UNGERLEIDER, M.D.

New York, New York

THE electrocardiogram as applied in clinical practice is used primarily as a diagnostic instrument. Prognosis is a prediction of future events from present signs. In forecasting the probable future of the patient with heart disease the electrocardiogram provides us with objective signs which have remote as well as immediate diagnostic application.

Those, like myself, who are engaged in life insurance medicine are concerned principally with the problem of prognosis, in other words, the ultimate mortality experience of the various impairments to which the human mechanism is subject. In evaluating the outlook in cardiovascular diseases, the electrocardiogram has assumed a most important role. During the past twenty-nine years, we have accumulated electrocardiograms of over 35,000 persons in the diagnostic laboratory at the Equitable Life Assurance Society of the United States and for the past several years we have been reviewing about 6,000 electrocardiograms annually submitted on applicants for insurance policies. The availability of long range follow up has made it possible for us to carry out a number of studies on mortality experience with various cardiac abnormalities, and particularly electrocardiographic abnormalities, some of which are reviewed here. Basically, there are three categories which fall within our scope: coronary disease, hypertrophy and cardiac irregularities.

It should appear a simple matter to catalog a list of electrocardiographic abnormalities and study these individually for the mortality experience. In certain instances, we have in fact been able to do this as will be indicated. However, it is not possible to treat the entire range of electrocardiographic abnormalities in this fashion. Some years ago, one of the large insurance organizations[1] undertook a mortality rating of each electrocardiographic finding separately, but it rapidly became evident that this was not only impractical, but thoroughly fallacious. The reasons for this are manifold. First, many electrocardiographic abnormalities occur, not as isolated findings, but rather as patterns. As one example we may cite the pattern of right ventricular hypertrophy in which right axis deviation is associated with T wave changes in leads II and III, and in which one must also consider multiple precordial leads. Another cause of difficulty is that many findings are of no consequence individually, but are non-specific and must be related to the general clinical picture. Such is the case with low voltage of the QRS complex which may be due to a large variety of causes, some entirely extracardiac in origin. In addition, there is a lack of unanimity in the definition of what constitutes an abnormality, as for example, slurring and notching of the QRS complex. Other abnormalities are difficult to identify with precision, as we learned from personal experience in attempting to carry out a study on the Q-T interval. The variations in the Q-T interval reported by the same trained analyst in reading the same electrocardiograms on successive occasions proved so great as to vitiate a study of the significance of variations in this interval. These unrelated examples illustrate the difficulties in any comprehensive studies, and indicate the necessity of approaching electrocardiographic interpretation statistically, as well as in clinical medicine, from the individual aspect, keeping clinical correlations constantly in mind. It must be remembered that the electrocardiogram reflects only one segment of the clinical picture, and that prognosis is not determined by the electrocardiogram as such, but by the underlying disease.

* From the North American Reassurance Company, New York, New York.

Coronary Artery Disease

Although changes in the coronary arteries are not a necessary or an integral part of advancing years, they are, in fact, almost universal. In a study carried out on 320 applicants for insurance policies a few years ago, employing roentgenographic and electrocardiographic criteria, we found evidence of arteriosclerotic changes in half of the men between the ages of fifty-one and fifty-five years and in 75 per cent of those above fifty-five years of age.[2] This accords well with the extensive pathologic studies of White, Edwards and Dry,[3] who demonstrated the presence of a severe grade of coronary artery sclerosis in over two-thirds of subjects above the age of fifty years. Viewed in this light, isolated electrocardiographic abnormalities in people above the age of fifty years become almost fortuitous findings. The clinical incidents which may punctuate changes in coronary arteries, such as coronary occlusion, are but the surface visible strata which may portend danger at the time of occurrence. Yet, as the work of Blumgart and co-workers[4] has shown, coronary occlusion often occurs unheralded by any clinical signs of illness. In either event, having once recovered from the acute and frequently critical phases of the attack, the future of the patient in respect to life expectancy and usually in relation to functional capacity as well, is not compromised by and dictated by the attack he has sustained but rather by further fortuitous changes in his coronary arteries. Within the past few years, two important studies[5] on life expectancy after attacks of coronary occlusion have been carried out in life insurance organizations. In both, the average life expectancy following the attack was approximately ten years. These cases are weighted adversely in comparison with the average case encountered in clinical practice, as data for these studies were drawn exclusively from disability experience; in other words, persons who were considered totally and permanently disabled three months following their attack. Certainly the outlook must be considerably more favorable when rapid functional recovery ensues, as is the situation in the vast majority of instances, and when patients are placed on a therapeutic regimen which may favorably influence their further course.

Acute Phases of Coronary Disease

It is well to inquire specifically how the electrocardiogram does and does not bear on the outlook in coronary artery disease. This is best viewed by individually surveying the several clinical syndromes of coronary disease.

Impending Myocardial Infarction: This is a relatively unappreciated but nevertheless important syndrome. On careful inquiry, a surprisingly large number of persons sustaining coronary attacks will give a history of vague and indefinite pain in the chest for some days or weeks antedating the actual attack. More important are patients who actually present themselves for examination with this complaint. The pain is by no means regularly typically anginal in nature, and unfortunately the electrocardiogram is usually normal. Although one might anticipate *a priori* that in such instances a provocative exercise test for evidence of coronary insufficiency would be informative, in our experience this has proved sadly disappointing. This is a situation in which the electrocardiogram more commonly than not fails prognostically even in predicting an immediately imminent event. Recognizing this, we may not rely too heavily on the electrocardiogram when our clinical judgment leads us to suspect that a coronary attack is impending. I digress to remark that in my opinion the prophylactic use of anticoagulants in this situation is probably more useful than when an attack already has occurred.

Acute Coronary Occlusion: When an attack of coronary occlusion occurs the electrocardiogram is our prime diagnostic instrument, but it does much more. It helps us prognostically in appraising not only the location but also the extent and severity of the attack and its evolution. Although clinical judgment is paramount and we have many signs to go by, the electrocardiogram is a useful guide to immediate mortality at the time of the acute attack. Some time ago, we carried out a study comparing electrocardiographic features in 100 patients with acute myocardial infarction without known antecedent heart disease of whom fifty survived and fifty died. There was a striking difference in the electrocardiographic patterns among the survivors as compared with those who died.[6] In brief, the majority of survivors exhibited an uncomplicated typical pattern either of anterior or posterior infarction; whereas among the group who died, forty-five of the fifty showed some complicating electrocardiographic abnormality in addition to the characteristics of anterior or posterior involvement.

Chief among these complicating features were the following: (1) evidence of combined anterior and posterior involvement; (2) presence of bundle branch block indicating septal involvement in addition to anterior or posterior infarction; (3) presence of Q waves across the entire precordium, indicative of extensive anterior infarction; (4) presence of a deep Q wave in lead I indicative of high anterior infarction in addition to the usual involvement of the apical area of the left ventricle; (5) marked deviations of the S-T segment beyond what is usually observed in acute anterior or posterior infarction; (6) progressive abnormality rather than improvement of the S-T segment; and (7) presence of major arrhythmias. Arrhythmias were found to be of graver consequence in anterior infarction. In posterior infarction they occur commonly and are often transitory.

Additional features observed more commonly in patients who died included tachycardia, very low voltage, progressive electrocardiographic changes other than the usual serial evolution, a predominantly upright QRS in lead aVR, electrical alternans, significant prolongation of the Q-T interval, very prominent P waves and abnormal depression of the P-R segment indicating auricular infarction. It is evident then that the electrocardiogram serves prognostic as well as diagnostic purposes in acute coronary occlusion. As has been observed repeatedly, there is no decided difference in outcome between infarction of the anterior and posterior wall.

Functional Recovery in Acute Coronary Occlusion: The electrocardiogram is serviceable prognostically in coronary occlusion not only at the time of the attack but also in evaluating recovery and ability to resume functional activity. For this purpose, the resting electrocardiogram is of no value, for it may be months before the typical serial changes in the electrocardiogram after an attack of acute infarction evolve to a stable pattern and it is unwarranted to keep the patient incapacitated while the changes are slowly evolving. We have applied the electrocardiographic response to exercise prognostically in assessing the degree of functional recovery following convalescence from acute myocardial infarction. If any considerable ischemia still remains, exercise will cause the reappearance of changes similar to those observed in the initial phases of the attack. However, if the patient has made a good functional recovery, the electrocardiogram will show no such marked changes following a moderate amount of effort. This seems a sensible procedure to employ in appraising the fitness to return to physical activity rather than to use arbitrary advice as is generally practiced. While it may appear that there is some element of risk in exposing a patient to exercise after recovery from a coronary attack, certainly it is much better to do this under supervision and actually observe what effects exercise has on the myocardium rather than allow him to undertake full activity without knowledge of its consequences.

Mild Myocardial Infarction: A distinctive syndrome which may be attended by a good immediate prognosis as well as a somewhat more favorable long term outlook comprises those patients, forming a not inconsiderable number, whose acute attacks are very mild. After an initial episode of pain in the chest which, although initially severe, may not be protracted, the clinical course may be entirely benign and laboratory data such as temperature, sedimentation rate and transaminase, may be inconclusive. Electrocardiograms are apt to exhibit only T wave changes which may not be major in degree or involve multiple leads, and such abnormalities as occur may regress completely within a few days or weeks. In a series of patients hospitalized with this pattern, presumably reflecting minor or focal infarction, the most common age group comprised persons in the late thirties and in the forties.[7] There were no deaths and functional recovery was uniformly good. However, the long term outlook cannot be considered benign, however minimal the acute attack. In one series of sixty-nine such patients[8] hospitalized with a slightly more severe pattern, but less than the classic attack of acute myocardial infarction, there were four deaths within the first month and three to four deaths annually over a five-year follow up. Forty-seven of sixty-five patients (72.3 per cent) survived for five years. The majority of deaths in the follow-up period were due to heart disease.

Ballistocardiogram in Coronary Occlusion: The ballistocardiogram is almost universally recorded with electrocardiographic apparatus, and has become a common adjunct in the examination of cardiac patients, particularly those with coronary disease. However, although the ballistocardiogram provides interesting physiologic information, in our experience, its actual clinical value has been limited.

TABLE 1
Mortality Ratios (Actual: Expected) in Coronary Heart Disease*

	Mortality (%)
Coronary occlusion (myocardial infarct)–good functional recovery, with minimal residua	
Under 60 years of age at time of attack	
0 to two years	Over 500
2 to 5 years	500
5 to 10 years	300
More than 10 years	200
Over 60 years of age at time of attack, or questionable or minimal episode of infarction	
1 to 5 years	300
5 to 10 years	200
Pain in the chest	
Anginal type	
Onset within one-year period, or severe in degree producing functional limitation or requiring frequent use of nitroglycerin, major electrocardiographic abnormality	500
Evidence of coronary insufficiency in exercise test	
Under 60 years of age	500
Over 60 years of age	300
No evidence of coronary insufficiency on double two-step exercise test	200 to 300
Atypical pain in the chest	
Not having anginal characteristics; results of electrocardiographic exercise test negative	100 to 200
Asymptomatic coronary disease (electrocardiographic abnormalities)	
Pattern of old infarction without history (Q wave abnormalities, etc.)	
Under 60 years of age	500
Over 60 years of age	300
Major T wave abnormalities	
Under 60 years of age	300 to 500
Over 60 years of age	200 to 300
Abnormal double two-step exercise test	
Ischemic S-T segment changes	
Under 60 years of age	300
Over 60 years of age	200
Junctional S-T segment or atypical changes	150 to 200
Minor T wave abnormalities	100 to 200
Bundle branch block	
Incomplete right, or other conduction anomaly	150 to 200
Complete right or left bundle branch block	200

* The term mortality ratio (ratio of actual: expected deaths) is infrequently used in clinical parlance, but serves the useful purpose of expressing the prognostic significance of a particular disorder in relation to another population, the standard of similar age and sex. This population may be insured persons charged the standard rate of premium, or the general population of a specified area and time. A mortality ratio of 100 per cent indicates that within a fixed period of time the proportion of deaths among those with the disorder in question is equal to the proportion expected to die according to the rates of mortality of the standard population. A mortality ratio of 150 per cent indicates that one and a half times the proportion of deaths expected in the standard population have occurred among those with the specified disorder. Insurability is generally limited to persons whose impairments are such that it is anticipated that they will not experience a long term mortality ratio exceeding 500 per cent, that is, will not exceed five times as many deaths as would occur in a similar group of standard lives.

Abnormal grades of ballistocardiograms occur so commonly beyond the age of forty-five to fifty years that very little diagnostic value can be attached to such abnormalities unless they be extreme. When there is any considerable tachycardia, the ballistocardiogram cannot be properly interpreted. Left ventricular activity, which is what interests us in coronary disease, is reflected only in the expiratory phase of respiration and if the ballistocardiogram is recorded with respiration suspended in inspiration the complexes almost invariably appear normal, for we are recording right rather than left ventricular activity. In patients with coronary occlusion, we have generally found the ballistocardiogram to be abnormal in older people after coronary attacks and we have generally found it to be substantially normal in younger people who have had coronary attacks.[9] This reflects the general age trend we observe

in the population at large. The fact that the ballistocardiogram so frequently remains normal after coronary attacks in younger persons serves to indicate that in most instances attacks of myocardial infarction do not greatly decrease the force or power of the heart. This affirms our clinical recognition that physical activity and performance are not generally severely compromised by coronary attacks.

CHRONIC CORONARY DISEASE

An even more important problem than the use of the electrocardiogram in prognosis of the acute phases of coronary artery disease is the evaluation of electrocardiographic abnormalities in chronic coronary disease which may be totally asymptomatic or may be attended by the symptoms of angina pectoris. In this situation, so common as we have already indicated in persons above the age of fifty years, the electrocardiogram usually provides the sole abnormality on examination. It is from the electrocardiogram that we must decide not only as to diagnosis but also the probable pattern of the patient's future (Table 1).

Asymptomatic Coronary Disease: Some data on survival in asymptomatic coronary disease have been gathered from mortality studies in patients with isolated electrocardiographic abnormalities presumably due to coronary disease, such as bundle branch block and T wave changes. In right or left bundle branch block as an isolated impairment, mortality was found to be surprisingly low, not greatly exceeding the expected mortality in a study at the Equitable Life Assurance Society of the United States. Experience with major T wave abnormalities is somewhat less favorable, as indicated by a long term follow up among employees at the Prudential Life Insurance Company.[5] Among a small number of persons with major T wave abnormalities the mortality ratio was approximately three and a half times that of a control group. A larger experience among persons with isolated minor T wave abnormalities (such as low amplitude in leads I, II, and left precordial leads) revealed a mortality twice that of the control group.

Prognostic Value of Exercise Test: An important prognostic, as well as diagnostic, aid in coronary disease is provided by the double two-step exercise test properly performed and interpreted. A follow-up study of 836 military personnel and 379 applicants for insurance policies in whom this test was carried out because of suspicion of coronary disease has been reported by Robb, Marks and Mattingly.[5b] In both groups the death rate in those who exhibited ischemic electrocardiographic changes after exercise was almost three times greater than in those whose test had given negative results, and there were more than six times as many deaths subsequently from acute coronary occlusion in those whose test had given an abnormal result. Persons with pain in the chest whose exercise tests gave negative results had virtually the same mortality experience as that for adult men of comparable age in the general population. Similar observations have been reported in studies employing the anoxemia test, in which there was a six- to seven-year follow up, although in another study more reserved conclusions were drawn concerning the prognostic value of this test.

Prognostic Significance of Bundle Branch Block: Several studies have been carried out on certain electrocardiographic abnormalities associated with chronic coronary disease, namely, bundle branch block and the Q wave in lead III. Some preliminary studies also have been carried out on the prognostic significance of other isolated findings such as T wave abnormalities.

Abnormalities in the ventricular complex are of several types. Widening of the QRS beyond 0.10 second is a definitely abnormal finding except in the precordial leads in which the QRS duration may normally attain 0.11 second. A more advanced expression of this abnormality is bundle branch block in which the width of the QRS exceeds 0.12 second, but within the past few years it has been recognized that not all types of bundle branch block carry an equally poor prognosis. A not uncommon type of atypical bundle block is encountered in which the widening is in the S wave, the so-called S_1 type of bundle branch block. This is indicative of organic heart disease, but apparently does not signify as extensive myocardial disease as the typical pattern of bundle branch block usually associated with considerable cardiac enlargement and diffuse myocardial disease. Another type of widened QRS pattern exists, which is presumably due to aberrant conduction from auricle to ventricle, the Wolff-Parkinson-White syndrome or bundle branch block associated with short P-R interval. Patients with this anomaly are subject to attacks of paroxysmal ventricular tachycardia, but are otherwise normal and do not have organic heart disease.

Nevertheless, we have observed several patients with a short P-R interval and widened QRS (conforming to the Wolff-Parkinson-White pattern) in whom definite hypertensive heart disease existed, and we are therefore reluctant to dismiss this abnormality lightly. Admittedly, it is a rare finding.

Some time ago we reported a study on the mortality of bundle branch block, comprising an analysis of 193 persons studied in the diagnostic laboratory of the Equitable Life Assurance Society.[10] The type of bundle branch block was classified as right in 131 patients, left in fifty-two, atypical in five and of the WPW type in five. It is of interest that the incidence of right bundle branch block is more common than that of left bundle branch block in the general population, particularly in younger age groups. The most significant finding in our study was the unexpected observation that bundle branch block in the absence of other cardiovascular abnormalities is not attended by a high mortality rate. In the past, bundle branch block has been regarded as of ominous portent, but our own study indicates that this is far from the truth and indeed we have now opened the possibility of insurance to such patients, properly selected.

Prognostic Significance of a Deep Q_3 Wave: A most important problem in regard to the QRS is the ever recurring question of the Q_3 wave. Although numerous studies have confirmed the pathologic significance of the Q wave in lead III as first described by Pardee, this sign still remains a subject of inquiry and some uncertainty. Occurring preponderantly in patients with organic heart disease, particularly coronary artery disease, Q waves conforming to Pardee's criteria of abnormality are seen also in certain normal persons, particularly in those whose heart lies transversely. In order to distinguish normal from pathologic Q waves in lead III, various modifications of Pardee's criteria have been recommended. Unipolar extremity leads, simultaneous registration of multiple limb leads and esophageal leads have been employed for this purpose.

Other problems complicate the interpretation of the Q wave in lead III. Among these are its anatomic basis, the significance of Q_3 waves when marked respiratory variation occurs, the significance of the small Q_3 wave not fully meeting Pardee's criterion of equaling or exceeding 25 per cent of the greatest amplitude of the tallest QRS in the limb leads, the propriety of accepting as an abnormal Q_3 complexes preceded in some beats by a small initial upward deflection, and the significance of the QS pattern in lead III and its relation to the Q_3 wave.

Recently we carried out an investigation in an attempt to resolve some of these questions by reviewing a large source of material which appeared uniquely suitable for such an analysis.[11] A total of 1,355 patients were studied in all of whom the records of history, physical examination and teleoroentgenogram were reviewed in addition to the electrocardiogram. A limited mortality study suggests strongly that the Q_3 wave deflection is a significant abnormality which should not be dismissed simply because of associated overweight and transverse position of the heart. Fifteen of seventeen patients with no cardiovascular abnormalities other than the abnormal Q_3 wave deflection succumbed to coronary disease with an average survival period for the entire seventeen patients of 5.7 years.

Significance of S-T and T Abnormalities: As already indicated, abnormalities of the S-T segment and T wave can be due to a great diversity of causes which do not necessarily signify organic heart disease. It is beyond the scope of this paper to consider these individually. However, in our opinion, the generally accepted abnormalities of this complex should be regarded as indicating organic myocardial involvement unless there is adequate proof to the contrary. A frequent problem is the differentiation of positional effects on the S-T segment and T wave from organic changes, e.g., asthenic persons who in the erect position may demonstrate low T waves in lead I and inverted T in leads II and III, and also inversion of the T wave in lead aVL and some precordial leads. The fact that abnormalities of the T wave can be made to disappear with position or vary with respiration should give us cause to dismiss such findings; even though from time to time all of us see bizarre cases with inversions of the T wave in any lead which we cannot explain or correlate with organic disease.

Adequate data on the ultimate prognosis, i.e., life expectancy with persons of various T wave abnormalities, are not available. For such studies to be carried out, a breakdown into a great number of groups becomes necessary involving consideration of the type of T wave abnormalities, the leads in which they occur, the age and body build, and the presence

or absence of associated abnormalities. These necessarily dilute sampling so that ultimate mortality experience in adequate numbers becomes difficult to obtain. Some indication that T wave abnormalities, even when not marked, are significant is provided from a study conducted among employees of the Prudential Insurance Company.[5] So minor a change as notching of the T wave was considered in this study to be indicative of a life expectancy category not much better than those of patients who had recovered from an acute myocardial infarction. Excluding notching of the T waves in the transitional zones of leads V_2 and V_3 it was found that more than three-quarters of the persons with definite notching of the T wave above the age of forty years had evidence of cardiovascular disease, and there were several fatalities in a limited follow up averaging slightly over four years in this group.

Another borderline finding, i.e., low T waves in leads V_5 and V_6 was similarly found to have an unfavorable outlook. Again, three-quarters of the persons with this abnormality had evidence of organic heart disease, which was two and a half times higher than the incidence of cardiovascular abnormalities among a control group with normal electrocardiograms. In this group, too, there were several fatalities in a follow-up period of four years whereas none occurred among the control group. A third borderline abnormality, inversion of the T wave in lead aVL, provided almost identical adverse experience in persons above the age of forty years. When the inverted T wave in lead aVL was associated with an upright QRS complex greater than 5 mm., not only was the evidence of organic heart disease much greater in this group than in the control subjects, but the fatalities in an average three-year follow-up period were also significantly higher.

In view of the unfavorable aspect of these borderline types of T wave abnormalities, it is evident that one must regard greater degrees of T wave abnormalities, such as inversion in leads I and II, and in the precordial leads, with greater concern. It is fair to regard persons with such abnormalities who are above the age of forty years in the same category as those who have recovered from myocardial infarction. Both have coronary artery disease and the future of such patients depends on the further progression of changes in their coronary arteries.

The mortality rate from coronary artery disease may be assessed from Table 1.

Cardiac Arrhythmias

Some arrhythmias of themselves carry an evidently poor prognostic import since they are of themselves hazardous. Others are important in that they provide a clue to the presence of organic heart disease and in such circumstances the prognosis must be appraised from whatever associated condition is present. In the first category are ventricular fibrillation and tachycardia, heart block, and under certain circumstances, auricular flutter and fibrillation. In the second category the most common arrhythmia is extrasystoles.

Extrasystoles: Some years ago we carried out an analysis of 1,142 applicants for insurance policies with extrasystoles or premature contractions.[12] In 58 per cent of the applicants with extrasystoles or premature contractions, no objective evidence of heart disease was found. In addition to physical examination and the electrocardiogram, fluoroscopic study or a teleoroentgenogram of the heart was made in most patients. Brachial pulse sphygmograms synchronous with the electrocardiogram were also recorded in a large number.

Analysis of this large series indicates that ventricular extrasystoles occur with considerably greater frequency than supraventricular premature contractions, and that in the presence of heart disease there is still greater preponderance of ventricular premature contractions. Several factors were found to increase the significance of premature beats. Among these are (1) occurrence of premature beats of multifocal origin; (2) frequent and persistent premature beats, particularly if they occur successively in short runs interrupting the regular rhythm; (3) a definite increase in the number or a "shower" of extrasystoles immediately following exercise; (4) occurrence of premature contractions in the presence of a rapid heart rate, i.e., over 90 per minute; (5) inversion of the T wave in the next regular beat which follows the extrasystole; and (6) postextrasystolic pulsus alternans. Any of these findings strongly suggest that extrasystoles are caused by organic heart disease.

A study carried out at the Prudential Life Insurance Company which comprised 476 patients with unifocal ventricular extrasystoles, 237 with unifocal supraventricular premature beats and eighty with multifocal premature

beats, led to the conclusion that persons above the age of forty years with extrasystoles should be viewed conservatively from a prognostic viewpoint. In this study it was found that 71 per cent of those above the age of forty years with extrasystoles had other indications of organic heart disease whereas in a comparable age group without ectopic beats only 32 per cent had evidence of cardiovascular abnormalities. There was a high incidence of cardiovascular deaths in an average follow up to 5.1 years, totaling 29 per cent of 372 patients with extrasystoles and other cardiovascular abnormalities, compared to a mortality rate of 2 per cent in a control group of comparable age. When multifocal extrasystoles were present, the mortality experience was also highly unfavorable. It was concluded on the basis of this study that the presence of extrasystoles, especially in older age groups, dictates a careful cardiovascular study.

Sinus Arrhythmias and Prolonged P-R Interval: A surprisingly high incidence of heart disease was also found in older persons with marked sinus arrhythmia and in both young and older persons who exhibited a wide P wave exceeding 0.11 second or abnormally high P waves, and also in persons with a prolonged P-R interval. It is evident that arrhythmias, which may be of themselves innocent, nevertheless often reflect the presence of organic heart disease. Particularly in older people one cannot, in view of this experience, dismiss cardiac irregularities lightly.

Cardiac Hypertrophy

Electrocardiographic Criteria for Left Ventricular Hypertrophy: It is not generally appreciated that the electrocardiogram is more sensitive than roentgenologic methods in detecting left ventricular hypertrophy. The electrocardiographic pattern of left ventricular hypertrophy or strain has long been recognized, but specific criteria indicating the point of departure from normal were not established prior to the analysis of 940 patients carried out in our laboratory. On the basis of this study, left ventricular hypertrophy may be considered to be present when left axis deviation occurs in association with any of the following changes: (1) increase in amplitude of the QRS complex, best expressed by the sum of R_1 and S_3. Hypertrophy is present if this sum exceeds 2.5 mv. and is probably present if it is over 2.2 mv. The increase in voltage is the earliest electrocardiographic change in hypertrophy. Subsequent to our study, electrocardiographic criteria for left ventricular hypertrophy have been elaborated by Sokolow and Lyon using QRS amplitude in unipolar extremity and precordial leads. These are somewhat more sensitive than the limb lead criteria of voltage, but less specific and sometimes are falsely positive. (2) Any perceptible depression of the S-T segment in lead I, even of as slight degree as 0.5 mm. (3) Lowering of T_1 below 1 mm. or further degree of abnormality of T_1.

The changes in the S-T segment and the T wave may develop in the absence of left axis deviation, and left axis deviation is not an invariable or necessarily integral part of the electrocardiographic pattern of left ventricular hypertrophy. The usual occurrence of left axis deviation with left ventricular hypertrophy in hypertension is due largely to predominant obesity with transverse position of the heart, which in itself causes left axis deviation. In slender subjects with left ventricular hypertrophy left axis deviation is not so frequently observed.

Electrocardiographic Signs of Left Ventricular Hypertrophy in Hypertension: Employing our criteria we found that evidence of left ventricular hypertrophy in the electrocardiogram was present considerably more often than roentgenologic changes in 100 subjects with advanced hypertensive disease.[13] Electrocardiographic and roentgenologic changes do not necessarily parallel one another. While electrocardiographic abnormalities occur relatively more frequently than roentgenologic changes, there also may be definite evidence of left ventricular enlargement in the roentgenogram while the electrocardiogram is normal. This is particularly the case when concurrent right ventricular enlargement is present, the opposite electrical effects of those chambers balancing one another. In analysis of 100 patients with advanced hypertensive disease, it was found that combined roentgenographic and electrocardiographic study revealed hypertrophy or arteriosclerotic changes in 90 per cent. The advantage of employing both procedures, therefore, is evident.

Electrocardiographic Signs of Left Ventricular Hypertrophy and Prognosis: The electrocardiographic patterns of left ventricular hypertrophy are of considerable prognostic importance. A few years ago we carried out a mortality study in an effort to determine whether electro-

cardiographic criteria for the detection of left ventricular hypertrophy and arteriosclerotic changes would allow classification of subjects with elevated deviations from normal blood pressure into distinct groups, regardless of actual blood pressure levels, and thus provide an index of the duration and stage of the hypertensive disease. This study was carried out with reference to the electrocardiographic findings and without consideration of the teleoroentgenogram, although the latter would have contributed much to the investigation.

The material for the study comprised 424 applicants for insurance policies who were examined in the diagnostic laboratory of the Equitable home office. In practically all applicants, the primary impairment which led to examination in the diagnostic laboratory was hypertension, but not of sufficient degree to cause declination as a single factor. Higher readings which, in themselves, would have dictated declination without further study were found, however, in a number of cases at the time of home office examination.

The electrocardiograms of those 424 subjects with hypertension were divided into four groups: (1) normal electrocardiogram; (2) borderline electrocardiogram; (3) pattern of left ventricular hypertrophy; and (4) evidence of myocardial disease with or without left ventricular hypertrophy. The data were tested for homogeneity as to age, build and blood pressure. They were found to be homogeneous with regard to age and build, and reasonably homogeneous with regard to blood pressure. The average blood pressure reading was 160/100 mm. Hg.

In view of the relative homogeneity of the factors of age, build and blood pressure, the increase in mortality from 186 per cent in those with normal electrocardiograms to 344 per cent in those with the pattern of hypertrophy must be considered as correlated with the conditions which caused the electrocardiographic changes which formed the criteria for the study. It is evident that in patients with hypertension who present the pattern of left ventricular hypertrophy, as defined by the criteria established in this study, the mortality becomes quite excessive and high extra premiums for insurance policies are necessary. Even the group with normal electrocardiograms has a mortality of 186 per cent, but these people are insurable with a relatively low extra premium. The conclusion appears warranted that the evaluation of the duration of hypertension based on the electrocardiogram is a valuable and important consideration in the prognosis and insurability of patients with hypertension.

The findings abundantly justify the employment of more detailed study in the presence of hypertension. Since the electrocardiogram was normal in only 44 per cent of 424 applicants with hypertension, it would appear worthwhile to record electrocardiograms routinely whenever the blood pressure is over 140 mm. Hg systolic and 90 mm. Hg diastolic.

Summary

The electrocardiogram has definite value prognostically as well as diagnostically in its major spheres of application, coronary disease, cardiac hypertrophy and the arrhythmias.

This paper reviews the prognostic significance and the effect on mortality statistics of these types of heart disease.

References

1. Bonnet, E. C. Notes on one method of underwriting electrocardiogram. *Proc. Life Ins. M. Dir.*, 26: 120, 1940.
2. Ungerleider, H. E. and Gubner, R. Blood lipids and human arteriosclerosis. *J. Michigan M. Soc.*, 1: 1360, 1938.
3. White, N. K., Edwards, J. E. and Dry, T. J. Relationship of the degree of coronary arteriosclerosis with age, in men. *Circulation*, 1: 645, 1950.
4. (*a*) Blumgart, H. L., Schlesinger, M. J. and Davis, D. Studies on relation of clinical manifestations of angina pectoris, coronary thrombosis and myocardial infarction to pathologic findings, with particular reference to collateral circulation. *Am. Heart J.*, 19:1, 1940.
   (*b*) Blumgart, H. L., Schlesinger, M. J. and Zoll, P. M. Angina pectoris, coronary failure and acute myocardial infarction. *J. A. M. A.*, 116: 91, 1941.
5. (*a*) Kreesling, C. E., Schaaf, R. S. and Lyle, A. M. Mortality studies of isolated electrocardiographic T wave changes. *Proc. Life Ins. M. Dir.*, 39: 5, 1955.
   (*b*) Robb, G. P., Marks, H. H. and Mattingly, T. W. Detection of coronary artery disease. *Proc. Life Ins. M. Dir.*, 40: 52, 1956.
6. Unpublished data.
7. Unpublished data.
8. Unpublished data.
9. Gubner, R., Rodstein, M. and Ungerleider, H. E. Ballistocardiography. *Circulation*, 7: 268, 1953.
10. Rodstein, M., Gubner, R., Mills, J. P., Lovell, J. F. and Ungerleider, H. E. A mortality study in bundle branch block. *Arch. Int. Med.*, 87: 663, 1951.

11. UNGERLEIDER, H. E. and GUBNER, R. The Q_3 and QS_3 deflection in the electrocardiogram. *Arch. Int. Med.*, 72: 196, 1943.
12. UNGERLEIDER, H. E. and GUBNER, R. Extrasystoles and the mechanism of palpitation. *Tr. Am. Therap. Soc.*, 42: 169, 1942.
13. GUBNER, R. S. and UNGERLEIDER, H. E. Electrocardiographic criteria of left ventricular hypertrophy. The factors determining the evolution of the electrocardiographic patterns in hypertrophy and bundle branch block. *Arch. Int. Med.*, 72: 196, 1943.

The Problem of Loss of Consciousness in Flying Personnel*

GEORGE DERMKSIAN, M.D.
New York, New York

LOSS OF consciousness is one of the more serious problems currently facing aviation and space medicine. Split-second human failure in the modern supersonic aircraft of today and the rocket-propelled space craft of tomorrow can have disastrous consequences. At ground level syncope is regarded quite casually by the lay public and the medical profession alike because of the usual lack of complications and sequelae. But in the environments of the atmosphere and space, transitory loss of conciousness is more likely to result in serious accidents with loss of life and property. Therefore, it becomes obvious that persons in primary control of aircraft must not be prone to syncope.

Although syncope is a common occurrence, little information is available concerning its incidence in the general population, in an apparently healthy adult male population and in flying personnel. More important, little is known concerning the likelihood of recurrence in any given subject, or the relationship of clinical syncope to experimental syncope. Criteria for selection of U. S. Air Force flying personnel are based upon an absence of syncopal episodes in the past and a rigorous physical examination. It is difficult to judge the adequacy of these technics for selection. However, they seem inadequate when an attempt is being made to determine whether or not a subject who has fainted at ground level is apt to have a similar episode during flight.

The School of Aviation Medicine studied 132 apparently healthy persons, ninety-seven with a history of clinical syncope and thirty-five without such a history. This survey provided an opportunity for reviewing the mechanisms resulting in syncope in apparently healthy people. It was believed that the incidence of such mechanisms would differ from that of the general population because of the initial selection criteria, and that such classic mechanisms as aortic stenosis,[1–3] anemia and central nervous system disorders[4] would account for little, if any, of the syncopal episodes in flying personnel.

MATERIAL AND METHODS

In an attempt to determine the true incidence of syncope in an apparently healthy population of young adult men, 5,000 questionnaires were sent to Air Force personnel on a single base. It was requested that the questionnaires be returned unsigned to avoid any motivation to withhold information. No attempts were made regarding further selection within this population.

Fifty aviation cadets in preflight training volunteered as subjects for a special medical study. As an incentive, each was given additional time off from duty. None knew that the study was related to loss of consciousness. All cadets had previously denied syncopal episodes in order to gain admittance to the flight training program. Each cadet was assigned a number which he selected from a hat. He was never identified by name and thus was guaranteed anonymity. The cadets were then asked to report in writing any past history of syncope and the circumstances surrounding any episode. The purpose was to obtain some idea as to the percentage of people entering the flying training program who had experienced syncopal episodes. It was also hoped that, with a battery of special tests designed to test the cardiovascular system, those cadets with a pre-existing history of syncope could be selected. The examiners did not know the cadet's history until the special tests had been completed.

An additional eighty-two apparently healthy, flying personnel who had experienced 113 syncopal episodes were also studied.

All 132 subjects were studied with a detailed history, complete physical examination, complete blood counts, erythrocyte sedimentation rate, fasting blood sugar, urinalysis, roentgenogram of the chest and electrocardiogram. Roentgenograms of the skull and additional studies were obtained as indicated when a history of syncope was noted.

* From the Department of Medicine, St. Luke's Hospital, New York, New York.

Special Tests: The fifty aviation cadets and fifty-five of the eighty-two flying personnel were studied with a battery of special procedures designed to test the cardiovascular system at rest and under stress. These studies included observations of the subject's pulse, blood pressure, electrocardiogram, signs and symptoms on a tilt table during (1) adjustment to being strapped on a tilt table in the vertical position; (2) breath-holding at maximum inspiration—in the vertical and horizontal positions; (3) rapid hyperventilation for one minute followed by breath-holding—in the vertical and horizontal positions; (4) bilateral, but not simultaneous, carotid sinus massage of fifteen seconds' duration—in the vertical position; and (5) a fifteen-minute orthostatic tolerance test on the tilt table.

Finally, a one-minute cold pressor test (hand immersed in water between 0° and 1°C.) was performed. The response to intravenous administration of atropine (0.8 to 1.2 mg.) was also studied in fifty-five cases.

Results

Previous History of Syncope: Of the 5,000 questionnaires sent to Air Force personnel, 60 per cent were returned. The age range of this population was seventeen to sixty-two years and the average was 29.1 years. The incidence of syncope in this population of apparently healthy male adults was 7 per cent. Loss of consciousness associated with severe physical trauma was noted in 4 per cent and both syncope and loss of consciousness due to physical trauma in 0.7 per cent.

Fifteen of the fifty (30 per cent) aviation cadets examined admitted to a previous undisclosed history of syncope. The cadets represented a relatively young age group. Their age range was from nineteen to twenty-seven years and the average was 21.1 years.

Precipitating Factors: The fifteen aviation cadets had experienced seventeen syncopal episodes and the eighty-two flying personnel had experienced 113. Of the total 130 episodes, approximately 13 per cent were associated with changes in position (orthostatic). Pain, breath-holding, psychic trauma and unknown factors preceded the syncopal episode in 9.5 per cent, respectively. Eight per cent of the cases occurred during prolonged standing and progressively smaller percentages were associated with injections (6.5 per cent), exercise (4 per cent), nausea (4 per cent), urination (4 per cent), a variety of illnesses (4 per cent), resting (3 per cent), hyperventilation (3 per cent), increased g force (2 per cent), alcohol (2 per cent), carotid sinus massage (1.5 per cent), blood donations (1.5 per cent), shaving (1.5 per cent) and trauma to the head (1.5 per cent). Less than 1 per cent of the cases were associated with coughing, sudden change in temperature and generalized seizures. Many of these factors were noted to occur simultaneously in any given syncopal episode and, in compiling these frequencies, an attempt was made to determine the predominant factor.

Incidence and Mechanisms of Experimental Syncope: Of the 105 subjects studied with special procedures, thirty-seven (35 per cent) had at least one episode of experimental syncope. An additional subject, not studied with the special procedures, had clinical syncope induced by stimulation of the external auditory canal and it was noted that syncope could be repeatedly induced by such stimulation. Syncope was associated on every occasion with a slow A-V nodal rhythm. Seventy of the 105 subjects studied had experienced clinical episodes of syncope. Twenty-four (34 per cent) of these seventy also had experimental syncope, whereas fourteen (40 per cent) of the thirty-five subjects without clinical syncope had experimental syncope.

Within the cadet population, of the fifteen subjects who later were noted to have clinical syncope, experimental syncope developed in seven. Thus, eight other subjects with a previous history of clinical syncope did not have experimental syncope. Fourteen cadets who had experimental syncope denied previous episodes of clinical syncope.

Of the thirty-eight cases of experimental syncope, twenty-six (68 per cent) were associated with a cardiac arrhythmia or a sudden marked decrease in cardiac rate (greater than 40 cycles per minute). Ten cases (26 per cent) were associated primarily with a fall in blood pressure and insignificant changes in the cardiac rhythm and rate, and two subjects (5 per cent) manifested cardiac arrhythmia and an almost simultaneous decrease in blood pressure. Of the twenty-six cases of cardiac arrhythmia associated with experimental syncope, fifteen (58 per cent) were induced by breath-holding in the upright position. Carotid sinus massage and hyperventilation followed by breath-holding with orthostasis, orthostasis alone and the cold pressor test accounted for the remainder of the arrhythmias in decreasing order of frequency. The following arrhythmias were associated with experimental syncope: marked sinus bradycardia, sinus arrest with nodal escape beats,

atrial rhythm, A-V dissociation, nodal rhythms, nodal tachycardia and asystole.

There were seventy-four episodes of cardiac arrhythmia or a sudden marked decrease in cardiac rate (greater than 40 cycles per minute) during the special procedures. Not all these arrhythmias were associated with syncope (approximately one-third were). Sixty-six of the seventy-four arrhythmias were induced by the vertical position and the following maneuvers: breath-holding, forty-one (55 per cent); carotid sinus massage, sixteen (22 per cent); hyperventilation followed by breath-holding, nine (12 per cent). The orthostatic tolerances test resulted in seven arrhythmias (9 per cent) and one (2 per cent) occurred during the cold pressor test.

Breath-holding was associated with the following arrhythmias: marked sinus bradycardia, atrial rhythm, atrial premature contractions, atrial fusion beats, first and second degree atrioventricular block, atrioventricular dissociation, nodal rhythms, ventricular premature contractions and asystole.

Effect of Atropine: In fifty-five subjects to whom intravenous atropine was administered and the breathing maneuvers repeated, there were no instances of arrhythmia. Administration of atropine prevented the development of arrhythmia with breathing maneuvers in persons who had previously experienced arrhythmia on one or more occasions. In some subjects impending syncope was prevented on several occasions by intravenous administration of atropine. One patient had experienced a clinical history of syncope associated with breath-holding and this maneuver had repeatedly resulted in syncope associated with arrhythmia. When atropine was given and breath-holding performed, the patient's cardiac rhythm did not change, the rate increased, and he did not lose consciousness. On two separate occasions impending syncope during breath-holding was prevented with rapid intravenous administration of atropine.

Comments

Incidence of Syncope: Syncope is a well recognized syndrome.[5] However, the literature usually limits comments relative to its incidence to such terms as "frequent" or "common." In 1956, Collins[6,7] administered a medical history questionnaire to 300 airmen at Lackland Air Force Base with a 100 per cent return; he reported a 22.3 per cent of syncope. In addition, in reviewing the applications of personnel for flight training over a period of one year, he found less than 1 per cent disqualified because of a history of syncope. He attributed this large discrepancy of incidence in two comparable groups to the withholding of information by the flying applicants, since a history of syncope was disqualifying for flight training. The present study would tend to confirm this conclusion, as fifteen (30 per cent) of the group of fifty aviation cadets studied admitted to a history of syncope prior to entering the flight training program when guaranteed anonymity.

With a personal interview technic, Guzman-Perry[8] obtained histories of 300 healthy male students at the undergraduate and postgraduate levels of training. In this population, he found a 15.5 per cent incidence of fainting.

It is well recognized that a number of valid statistical objections can be raised regarding some of the incidence surveys mentioned herein. Studies having complete return of all questionnaires with anonymity assured can be statistically evaluated by applying the principles of sampling variation. In the fifty cadets surveyed here there is only one chance in twenty that the true incidence of previous syncope is less than 19 per cent or over 42 per cent. Indeed, the incidence of clinical syncope was 30 per cent in this group.

Since the incidence survey conducted in this study of apparently healthy persons on one military base did not have a 100 per cent return, the statistical analysis is not valid. Nevertheless, it is interesting when compared to the previously reported studies.[6-8] The 8 per cent figure noted in this population would seem to be at variance with such studies. But if the 4 per cent incidence of loss of consciousness due to physical trauma is included with the total incidence figure, which the other studies did, then the incidence becomes 12 per cent. If the increased age of this population as compared to the previous studies is taken into account, and it is assumed that memory for the remote past decreases with increasing age, then it can be seen that the 12 per cent incidence figure in this study is still somewhat lower than might be expected. This assumption would seem valid since 65 to 70 per cent of syncopal and loss of consciousness episodes occurred before the age of twenty-one years.[9,10]

Effect of Age: The progressively decreasing incidence of syncope and loss of consciousness with increasing age would seem to suggest an "increased resistance" to syncope with ad-

vancing age. This increased resistance to syncope could be due to a more stable cardiovascular system with increasing age or to a "learning process." Evidence for a more stable cardiovascular system is noted in the electrocardiographic survey conducted on 67,375 subjects by the School of Aviation Medicine.[11] There the incidence of passive supraventricular arrhythmias, as evidence of vagotonia, was noted to be more frequent in youth. The evidence for a learning process also seems well established, especially in syncope associated with psychic trauma. Romano et al.[12] studied decompression sickness and syncopal reactions during simulated exposure to high altitude in a decompression chamber. Of seventy-eight subjects, syncope developed in 18 per cent on the first flight. With subsequent flights the incidence of syncope decreased, although the incidence and severity of decompression sickness remained the same. By the seventh flight, the incidence of syncope was 2 per cent. Thus, learning and a more stable cardiovascular system seem to be two factors associated with the decreased incidence of syncope with increasing age in the apparently healthy person.

Mechanisms of Syncope: More than one mechanism may be involved in any given episode of syncope. Loss of peripheral arteriolar resistance and/or a cardio-inhibitory response probably account for most clinical episodes of syncope in apparently healthy persons.[10]

1. Inadequate venous return to the left side of the heart by pooling of blood in the systemic or pulmonary circulation may result in syncope due to a temporary decrease in left ventricular output. Large varicosities of the lower extremities,[13,14] decreased venous and arteriolar tone associated with orthostatic hypotension,[15–17] positive g forces,[18] pressure breathing, coughing,[19] deep inspiration[9,10] and the Valsalva maneuver are some of the factors which may result in trapping of blood peripherally and centrally. In reviewing the 130 clinical episodes of syncope, it may be noted that venous mechanisms could be implicated in a large percentage of these episodes along with cardiac and arteriolar factors.

2. Disturbances in the muscular pumping action of the heart may result in syncope. Diseases of the endocardium,[1–3,30] myocardium[4,5,21] and pericardium,[22] as well as a variety of arrhythmias,[5,9,10,23–25] can result in a decreased cardiac output and loss of consciousness.[26] In this healthy young adult male population it could be expected that the incidence of syncope secondary to cardiac disease would be quite low due to initial screening procedures and subsequent routine physical examinations. This is borne out by the absence of a single episode of syncope which could be attributed to detectable heart disease.

Significance of Cardiac Arrhythmia: The number of clinical episodes of syncope in this study that might have been due to or contributed to by a cardiac arrhythmia is unknown since the cardiac rhythm at the time of syncope was not recorded. However, in evaluating the cardiovascular system of the 105 subjects studied, it may be noted that of the thirty-eight cases of experimental syncope, cardiac arrhythmia was a feature in twenty-eight.

The significance of cardiac arrhythmias as a mechanism of syncope in apparently healthy persons had not been stressed in the literature until recently.[9,10] As a mechanism of syncope in organic heart disease it is well recognized, e.g., Adams-Stokes syndrome,[20,27] ventricular arrhythmias[28] and asystole.[29] One reason for this lack of emphasis on arrhythmias in apparently healthy persons is the infrequency with which we are able to document cardiac rhythm during clinical syncope. Another is the use of atropine and sodium nitrite in studying experimental syncope.[30,32] Atropine has a vagolytic action and abolishes cardiac arrhythmias associated with vagotonia. Administration of sodium nitrite produces a vasodepressor type of syncope with insignificant changes in cardiac rhythm. In this study a high incidence of arrhythmia was noted because atropine was not administered until many of the special procedures had been completed. That a large variety of arrhythmias may be associated with syncope is evident from these studies. A sudden change in rhythm with a sudden decrease in cardiac output resulting in cerebral hypoxia is one of the reasons for syncope. Another is the decrease in cardiac output associated with loss of peripheral arteriolar resistance. The cumulative effect of this combination is probably the most potent and most common mechanism of clinical and experimental syncope.

The largest percentage (55 per cent of seventy-four cases) of arrhythmias, with or without syncope, in this study was produced by breathing maneuvers, i.e., breath-holding in the upright position. However, such maneuvers as carotid sinus massage and orthostatic tests, which are classically associated with vasodepressor re-

sponses, accounted for 22 and 9 per cent, respectively, of the arrhythmias with and without syncope. This fact is interesting when one considers that these subjects had no evidence of cardiac disease and it also emphasizes the importance of cardiac arrhythmias in syncope.

Reflex Pathways for Cardio-inhibitor and Vasodepressor Responses: All maneuvers which resulted in cardiac arrhythmias appear to be mediated through a common reflex pathway, in which the glossopharyngeal and vagus nerves play a major role. The pathways have been well defined anatomically and adequately described.[33,35] The respiratory maneuvers, primarily inspiration, stimulate stretch receptors in the tracheobronchial tree, peripheral pulmonary parenchyma and the visceral and parietal pleura (pulmonary stretch reflex).[9] Impulses are carried by vagal visceral afferent fibers to the medulla. The carotid sinus contains special nervous end organs which convey pressure stimuli via the carotid branch of the glossopharyngeal nerve to the medulla. Similar receptors are located in the wall of the aortic arch and in the right subclavian and innominate arteries. The afferent fibers run in the aortic depressor nerve to the vagus and to the medulla. The efferent arc of these reflexes is mediated via vagal autonomic fibers to the cardiac plexus, and from there postganglionic fibers terminate in the sinoatrial and atrioventricular nodes. The primary effect of the right vagus on the sinoatrial node is to depress impulse formation there, and the left vagus decreases the relative refractory period of the atrioventricular node. Since all three reflexes are influenced by neurons from the respiratory, vasopressor and vasodepressor centers in the medulla, it can be seen how eliciting of these reflexes can cause a cardio-inhibitory and/or a vasodepressor response. There probably are other organ receptors and afferent pathways in addition to those mentioned, but the efferent arc resulting in the cardio-inhibitory or vasodepressor responses remains via the vagus nerve.

When the cardiac rate is rapid the autonomic control of the circulation is dominated by the sympathetic component. Stresses such as prolonged breath-holding, severe physical exercise or acceleration may induce such a response. As the stress is terminated, autonomic control may shift and the parasympathetic component may become dominant. In certain susceptible persons this can result in passive rhythms or marked bradycardia with a precipituous fall in cardiac rate. This phenomenon is called vagal rebound.

Breath-holding seems to be a particularly potent method of stimulating cardio-inhibitory responses. The intravenous administration of therapeutic doses of atropine (0.8 to 1.2 mg.) has been shown to prevent and abolish the cardio-inhibitory response to breath-holding in all susceptible persons.

In reviewing the factors associated with the 130 clinical episodes of syncope it can be seen that cardio-inhibitory and vasodepressor responses may have been frequently associated mechanisms resulting in syncope. This fact and the frequency with which such responses were noted in experimental syncope in this series would suggest that cardiac arrhythmias play a more important role in inducing or contributing to clinical syncope than has been previously suspected.

Respiratory Maneuvers and Syncope During Flight: In the light of the demonstrations that cardiac arrhythmias may result in syncope more frequently than previously suspected, and in view of the potency of the respiratory maneuvers, i.e., breath-holding in inducing cardiac arrhythmia in susceptible persons, it can readily be seen that such knowledge would have direct application to any activity involving respiratory maneuvers. This is especially so in aviation and space medicine where artificial aids to respiration, such as pressure breathing, may trigger a cardiac arrhythmia and result in syncope and death. Hyperventilation associated with anxiety, with exposure to altitude or as occurring in even the most experienced pilots in high performance aircraft during certain critical periods of flight,[36] may result in symptoms which the pilot may attempt to control by breath-holding. In the susceptible person, an arrhythmia, syncope and death can result. The M1 maneuver (forceful expiration against a partially closed glottis), which is used to increase the pilot's positive g tolerance, if improperly performed may have the same disastrous consequences as breath-holding and/or the Valsalva maneuver, i.e., cardiac arrhythmia and/or the trapping of blood peripherally and loss of consciousness.

In addition to its relevance in aviation and space medicine, the role of vagal reflexes becomes an important consideration in sudden death in healthy young adults, such as those associated with severe physical exertion, athletics (particularly underwater swimming and diving) and

fright. Cardiac arrest in the operating room may be due to intubation procedures or artificially controlled respiration by the anesthesiologist which stimulate the pulmonary stretch reflex. This reflex is usually not blocked by small preoperative doses of atropine (0.4 mg. administered parenterally). The initiation of micturition and paroxysms of coughing may also result in syncope by stimulation of the pulmonary stretch reflex, in addition to other suspected mechanisms.[19,37,38]

3. Vasodepressor Syncope: Loss of peripheral arteriolar resistance is a well recognized physiologic mechanism resulting in syncope (vasodepressor syncope). Many authors[4,5,45] consider this the most common type of syncope. This is suggested by the factors associated with the 130 clinical episodes reviewed here and in twelve of the thirty-eight experimental syncopal episodes. Vasodepressor syncope has been one of the best studied of all types of syncope.[4,39,40] Psychic trauma or stress with inability of the subject to respond with "flight or fight" is a frequent precipitating factor in this type of syncope. The previously described reflexes, in addition to producing cardio-inhibitory responses, may produce vasodepressor responses. Pain,[41] alcohol,[42] true orthostatic hypotension,[16] febrile illnesses, bed rest,[43] heat, exhaustion,[44] and fear[41] may also cause marked diminution of peripheral arteriolar resistance. Obviously many of these factors may be involved in loss of consciousness in flying personnel. In addition, positive g forces tend to overcome normal arteriolar resistance. A force of 5 to 6 g applied parallel to the longitudinal axis of the body results in loss of consciousness in most persons unless specially protected. It is important to remember that cardio-inhibitory responses may accompany loss of arteriolar resistance and the cumulative effect of both may result in syncope, whereas either one alone may not.

4. Syncope Due to Changes in Blood: Qualitative and quantitative changes in the circulating blood and its constituents is a fourth mechanism which may result in or predispose to syncope. Qualitative changes would include such factors as toxins, hypoxia or anoxia, hypoglycemia, hypercapnia and aberrations in acid-base and electrolyte balance. Quantitative changes in the blood which could induce syncope would include acute or chronic blood loss resulting in decreased circulating volume and/or decreased mass of red cells. Dehydration from any cause may result in a decreased circulating volume and result in syncope. Urination, resulting in collapse of a distended bladder, may result in sudden dilatation of the vascular bed and a relative decrease in circulating blood volume followed by syncope.

In this series of 130 clinical episodes of syncope, qualitative and quantitative changes in blood alone were suspected or found to be infrequent causes of syncope. Such changes in the blood are rarely severe enough by themselves to result in loss of consciousness. Usually they lower the subject's threshhold to syncope, so that an additional minor stress will result in syncope. For example, severe hypoglycemia (blood sugar less than 40 mg. per cent) will usually result in loss of consciousness, but less severe hypoglycemia is more frequently associated with disturbances in mental state and predisposes toward syncope.[45] Qualitative or quantitative changes alone in the blood usually result in syncope by direct action on the central nervous system or indirectly through the cardiovascular system.

5. Syncope Due to Abnormalities of Nervous System: Abnormalities of the central and peripheral nervous systems are another mechanism which may be involved in clinical syncope. This would include vascular anomalies resulting in hemorrhage, also hemorrhage associated with hypertension and trauma, cerebral thromboses, tumors, infections, metabolic and convulsive disorders and other disease of the brain, spinal cord and peripheral nerves. Such abnormalities may result in syncope directly through action on the central nervous system or indirectly through the cardiovascular system.[46–48] In two cases of experimental syncope in which electroencephalographic studies were performed simultaneously with the electrocardiogram and blood pressure observations, it was clearly evident that cardiac arrhythmias produced changes in the circulatory dynamics before electroencephalographic changes were noted.

In the series of 130 episodes of syncope reviewed, there was only one case due to an abnormality of the nervous system, and that was a generalized seizure disorder of undetermined etiology. Neurologic examination, including the electroencephalogram with provocative studies, failed to disclose any abnormality, and it was only through a subsequent observation of another seizure that the diagnosis was made. This low incidence of loss of consciousness due to a seizure disorder seems compatible with

the 0.5 per cent figure quoted for the general population.[49] Again the low incidence of neurologic disorders resulting in syncope in this study is due to the initial selection technics for this population.

In addition to the vasodepressor and cardio-inhibitory type of syncope associated with carotid sinus massage, Weiss and co-workers[50,51] described a type of cerebral syncope during which there was no change in cardiac rate, rhythm and blood pressure. Administration of atropine and epinephrine had no effect on the episode of syncope. They hypothesized two possible mechanisms: (1) cerebral arterial spasm and (2) a reflex to cerebral centers associated with unconsciousness. In this series, there was one similar case of experimental syncope.

Procedures to Determine Susceptibility to Syncope

One of the purposes of this study was the hope that the special procedures used to stress the cardiovascular system would aid in differentiating those subjects who had experienced clinical syncope from those who had not. It was thought that the group of cadets would be best suited for this part of the study since it could serve as its own control group and there was no prior knowledge regarding clinical syncope in any given subject. Since 45 per cent of the cadets with a clinical history of syncope had experimental syncope (55 per cent who had clinical syncope did not have experimental syncope) and 40 per cent without clinical syncope had experimental syncope, it was obvious that the response to the special procedures could not be correlated with the clinical history, and as such the studies had no predictive value. Similar conclusions are obtained when the fifty-five flying personnel are compared with the thirty-five cadets without a clinical history of syncope.

One of the problems in using any test procedure to determine susceptibility to syncope is individual variation from day to day. Fatigue, poor hygienic habits, emotional stress and other temporary situations may cause transitory susceptibility to clinical and experimental syncope. These factors may not be present during subsequent test procedures.

To test the clinical observation[9] that the incidence of syncope decreases with age, the incidence of experimental syncope in the cadets (average age 21.1 years) was compared with that in the flying personnel (average age 29.1 years). The incidence of experimental syncope in the younger cadets was 42 per cent as opposed to 25 per cent in the older flying personnel. This supports the proposition of decreasing incidence with increasing age, perhaps due to non-specific learning process in some and to change in autonomic control of the circulatory system in others.

Summary and Conclusions

A healthy young adult male population was surveyed in an attempt to determine the incidence of clinical syncope. The factors associated with 130 episodes of clinical syncope were reviewed in an attempt to determine their frequency. One hundred five subjects (seventy with and thirty-five without clinical syncope) were studied with special procedures designed to stress the cardiovascular system and determine the cardiovascular mechanisms resulting in experimental syncope. In addition, it was hoped that such procedures might distinguish those subjects with clinical syncope and thus have predictive value.

Thirty per cent of the aviation cadets were found to have had previous episodes of syncope.

The known factors most frequently associated with clinical syncope were orthostatic influences, pain, breath-holding or deep breathing, psychic trauma and prolonged standing. Frequently more than one factor contributed to the syncopal episode.

The special cardiovascular stresses revealed a surprisingly high incidence of cardiac arrhythmias in normal healthy adult men. These were most frequently produced by breath-holding in the vertical position and ranged from marked sinus bradycardia to asystole. Of the thirty-eight cases of experimental syncope 68 per cent were associated with an arrhythmia. It was thought that the arrhythmias were secondary to cardio-inhibitory responses mediated through the vagus nerve. They could be abolished or prevented with intravenous administration of atropine.

The special procedures failed to distinguish between persons with previous syncope and those without, and thus had no predictive value.

References

1. Gallavardin, L. Syncope from effort in aortic stenosis: frequency and diagnosis. *Arch. mal. coeur*, 30: 745, 1937.
2. Marvin, H. M. and Sullivan, A. G. Clinical observations upon syncope and sudden death in rela-

tion to aortic stenosis. *Am. Heart J.*, 10: 705, 1935.
3. McGinn, S. and White, P. D. Clinical observations on aortic stenosis. *Am. J. M. Sc.*, 188: 1, 1934.
4. Engel, G. L. Fainting. Physiologic and Psychologic Considerations, p. 52. Springfield, Ill., 1950. Charles C Thomas.
5. Weiss, S. Syncope and related syndromes. *Oxford Med.*, 2: 250, 1935.
6. Collins, T. A. An evaluation of current USAF policy in regard to management of disturbances of consciousness. Aviation Medicine Resident's Thesis, School of Aviation Medicine, USAF. San Antonio, Texas. May 1956.
7. Collins, T. A. The significance of loss of consciousness. In: Symposium on Physical Standards and Selection, School of Aviation Medicine, USAF. San Antonio, Texas. February 1957.
8. Guzman-Perry, C. J. Studies of syncope. Personal communication.
9. Dermksian, G. and Lamb, L. E. Syncope in a population of healthy young adults: incidence, mechanisms and significance. *J.A.M.A.*, 168: 1200, 1958
10. Dermksian, G. and Lamb, L. E. Cardiac arrhythmias in experimental syncope. *J.A.M.A.*, 168: 1623, 1958.
11. Fosmoe, R. J., Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. II. Supraventricular arrhythmias. *Am. J. Cardiol.*, 6: 84, 1960
12. Romano, J., Engel, G. L., Webb, J. P., Ferris, E. B., Ryder, H. W. and Blankenhorn, M. A. Syncopal reactions during simulated exposure to high altitude in the decompression chamber. *War Med.*, 4: 475, 1943.
13. Chapman, E. M. and Asmussen, E. On the occurrence of dyspnoea, dizziness, and precordial distress occasioned by the pooling of blood in varicose veins. *J. Clin. Invest.*, 21: 393, 1942.
14. Ebert, R. V. and Stead, E. A., Jr. The effect of the application of tourniquets on the hemodynamics of the circulation. *J. Clin. Invest.*, 19: 561, 1940.
15. Bradbury, S. and Eggleston, C. Postural hypotension. *Am. Heart J.*, 1: 73, 1925.
16. Stead, E. A., Jr. and Ebert, R. V. Postural hypotension, a disease of the sympathetic nervous system. *Arch. Int. Med.*, 67: 546, 1941.
17. MacLean, A. R., Allen, E. V. and Magath, T. B. Orthostatic tachycardia and orthostatic hypotension: defects in the return of venous blood to the heart. *Am. Heart J.*, 27: 145, 1944.
18. Mayerson, H. S. and Burch, G. E. Relationship of tissue (subcutaneous and muscular) and venous pressures to syncope induced in many by gravity. *Am. J. Physiol.*, 128: 258, 1939.
19. McCann, W. S., Bruce, R. A., Lovejoy, F. W., Jr., Yu, P. N. G., Pearson, R., Engel, G. and Kelly, J. Observations on a case of tussive syncope. *Tr. A. Am. Physicians*, 62:116, 1949.
20. Stokes, W. Observations on some cases of permanently slow pulse. *Dublin Quart. J. M. Sc.*, 2: 73, 1846.
21. Golden, A. Syncope associated with exertional dyspnea and angina pectoris. *Am. Heart J.*, 28: 689, 1944.
22. Wood, P. Diseases of the Heart and Circulation, 2nd ed., p. 657. Philadelphia, 1956. J. B. Lippincott Co.
23. Wolf, L. The cardinal manifestations of paroxysmal tachycardias: vascular collapse. *New England J. Med.*, 232: 527, 1945.
24. Corday, E., Gold, H., deVera, L. B. and Williams, J. H. The effect of cardiac arrhythmias on the coronary circulation. *Ann. Int. Med.*, 50: 535, 1959.
25. Corday, E., Williams, J. H., deVera, L. B. and Gold, H. Hemodynamics of the cardiac arrhythmias. *Mod. Concepts Cardiovas. Dis.*, 27: 493, 1958.
26. Agress, C. M. and Binder, M. J. Cardiogenic shock. *Am. Heart J.*, 54: 458, 1957.
27. Adams, R. Cases of diseases of the heart. *Dublin Hosp. Rep.*, 4: 353, 1827.
28. Schwartz, S. P. and Jezer, A. Transient ventricular fibrillation. The clinical and electrocardiographic manifestations of the syncopal seizures in a patient with A-V dissociation. *Arch. Int. Med.*, 50: 450, 1932.
29. Levine, S. A. and Malton, M. Observations on a case of Adams-Stokes syndrome, showing ventricular fibrillation and asystole lasting five minutes, with recovery following the intracardiac injection of adrenaline. *Heart*, 12: 271, 1926.
30. Weissler, A. M., Warren, J. V., Estes, E. H., Jr., McIntosh, H. D. and Leonard, J. J. Vasodepressor syncope. Factors influencing cardiac output. *Circulation*, 15: 875, 1957.
31. Weissler, A. M., Leonard, J. J. and Warren, J. V. Effects of posture and atropine on cardiac output. *J. Clin. Invest.*, 36: 1656, 1957.
32. Weiss, S., Wilkins, R. W. and Haynes, F. W. The nature of circulatory collapse induced by sodium nitrite. *J. Clin. Invest.*, 16: 73, 1937.
33. Goss, C. M. Gray's Anatomy of the Human Body, 25th ed., pp. 882, 936. Philadelphia, 1949. Lea and Febiger.
34. Lamb, L. E. Cardiac function and disease in acute and chronic exposure to altitude. *GP*, 17: 88, 1958.
35. Lamb, L. E., Dermksian, G. and Sarnoff, C. A. Significant cardiac arrhythmias induced by common respiratory maneuvers. *Am. J. Cardiol.*, 2: 563, 1958.
36. Dermksian, G. Unpublished observations.
37. Proudfit, W. and Forteza, M. E. Micturition syncope. *New England J. Med.*, 26: 328, 1959.
38. Dermksian, G. Further note on micturition syncope. *New England J. Med.*, 26: 1044, 1959.
39. Engel, G. L., Romano, J. and McLin, T. Vasodepressor and carotid sinus syncope. Clinical, electroencephalographic, and electrocardiographic observations. *Arch. Int. Med.*, 74: 100, 1944.
40. Engel, G. L. and Romano, J. Studies of syncope. IV. Biological interpretation of vasodepressor syncope. *Psychosom. Med.*, 9: 288, 1947.
41. Cannon, W. B. Bodily Changes in Pain, Hunger, Fear and Rage, 2nd ed., p. 104. New York, 1939. Appleton-Century-Crofts.
42. Goodman, L. S. and Gilman, A. The Pharmacological Basis of Therapeutics, 2nd ed., p. 99. New York, 1955. Macmillan Co.
43. Rusk, H. A. Convalescent training program. *Air Surgeon's Bull.*, 1: 14, 1944.

44. Eichna, W. A., Horvath, S. M. and Bean, W. B. Post exertional orthostatic hypotension. *Am. J. M. Sc.*, 213: 641, 1947.
45. Warren, J. V. Why people faint. *GP*, 6: 72, 1952.
46. MacLean, A. R. and Horton, B. T. Myasthenia gravis with postural hypotension. *Proc. Staff Meet. Mayo Clin.*, 13: 21, 1938.
47. Rundles, R. W. Diabetic neuropathy. *Medicine*, 24: 111, 1945.
48. Ellis, L. B. and Haynes, F. W. Postural hypotension with particular reference to its occurrence in disease of the central nervous system. *Arch. Int. Med.*, 58: 773, 1936.
49. Penfield, W. and Erickson, T. C. Epilepsy and Cerebral Localization, p. 310. Springfield, Ill., 1941. Charles C Thomas.
50. Weiss, S and Baker, J. P. The carotid sinus reflex in health and disease. Its role in the causation of fainting and convulsion. *Medicine*, 12: 297, 1933.
51. Ferris, E. B., Capps, R. B. and Weiss, S. Carotid sinus syncope and its bearing on the mechanism of the unconscious state and convulsions. *Medicine*, 14: 377, 1935.

Telemetering Physiologic Responses During Experimental Flights*

NORMAN LEE BARR, M.D. *and* ROBERT B. VOAS, PH.D.

Farmingdale, New York Langley, Virginia

MODERN technology has made it possible to transmit to remote locations nearly all physiologic responses which involve external electrical, mechanical or thermal changes. Since 1947 the Bureau of Medicine and Surgery has been sponsoring a project on "the transmission of physiological responses from air to ground by electronic methods." Under the program, equipment has been developed for telemetering a large variety of physiologic responses of persons in aircraft under operational conditions, especially those participating in hazardous experimental flights.

TELEMETERING SYSTEMS

Figure 1 presents in diagrammatic form the basic equipment required for telemetering physiologic responses. The electrical changes picked up or produced by the electrodes, thermistors and strain gauges are amplified and fed through subcarrier oscillators. This procedure imposes the voltage changes from each of these transistors on separate carrier frequencies which are then mixed or combined and after a further stage of amplification transmitted over a standard UHF frequency. At the ground station this transmission is picked up by a receiver, amplified once again and then the subcarrier frequencies are unscrambled by the use of a discriminator for each item of information. This information can then be presented on an oscilloscope, over a speaker or by means of an ink writer. If a speaker or ink writer is used a further stage of amplification is required. All data can be permanently stored by recording the signals prior to putting them through the disciminator. Physiologic responses from pilots beyond the radio range of the home station can be monitored by relaying information from remote stations to the home station by means of telephone lines. This additional relay procedure permits the recording of physiologic responses from any point on Earth which is within the range of one radio station.

Technical Problems: The transmission of responses over radio lengths involves a number of problems not encountered in laboratory electrophysiologic recording. Space does not permit a full discussion of these problems; however, several of the primary problems should be mentioned. The vibration of the plane and the activity of the pilot often make the securing of electrodes more difficult than under normal laboratory circumstances. It is also not possible to electrically shield the subject; therefore electronic noises interfere with the recording. All electronic equipment must be adapted for the aircraft's power supply. In addition, since this power supply is less stable than that usually available on the ground, special filtering must be developed. Another significant problem is the width of the carrier band. The frequency width of the carrier determines the maximum range of frequencies which can be transmitted. Several physiologic responses can be placed on the same carrier frequency if, as in the case of the electroencephalogram and the electrocardiogram, they have limited frequency ranges. On the other hand where a broader spectrum of frequency occurs, such as in the electromyogram, fewer measures can be sent with the same carrier frequency. Another problem not generally encountered in the laboratory is that of the size and weight of the equipment. The equipment must fit within the aircraft. Miniaturization of electrical components has brought this problem fairly close to solution. Where necessary, the weight and space requirements of electronic equipment can be reduced so that they become a minor factor. Radio transmission during poor weather conditions introduces noise into the system. To minimize this, FM transmission is used. A final difficulty in remote recording is that in the case of a poor recording it is not possible to check the leads and connections on the pilot immediately and it is sometimes difficult to determine the cause of any malfunction. Despite these many problems, electrophysiologic responses of varied types have been successfully transmitted for long distances by radio equipment. With equipment developed under this program, it is possible to transmit into the laboratory almost any electrophysiologic response which can be recorded.

* From the Aeronautical Division, Bureau of Medicine and Surgery, Department of the Navy, Washington, D. C.

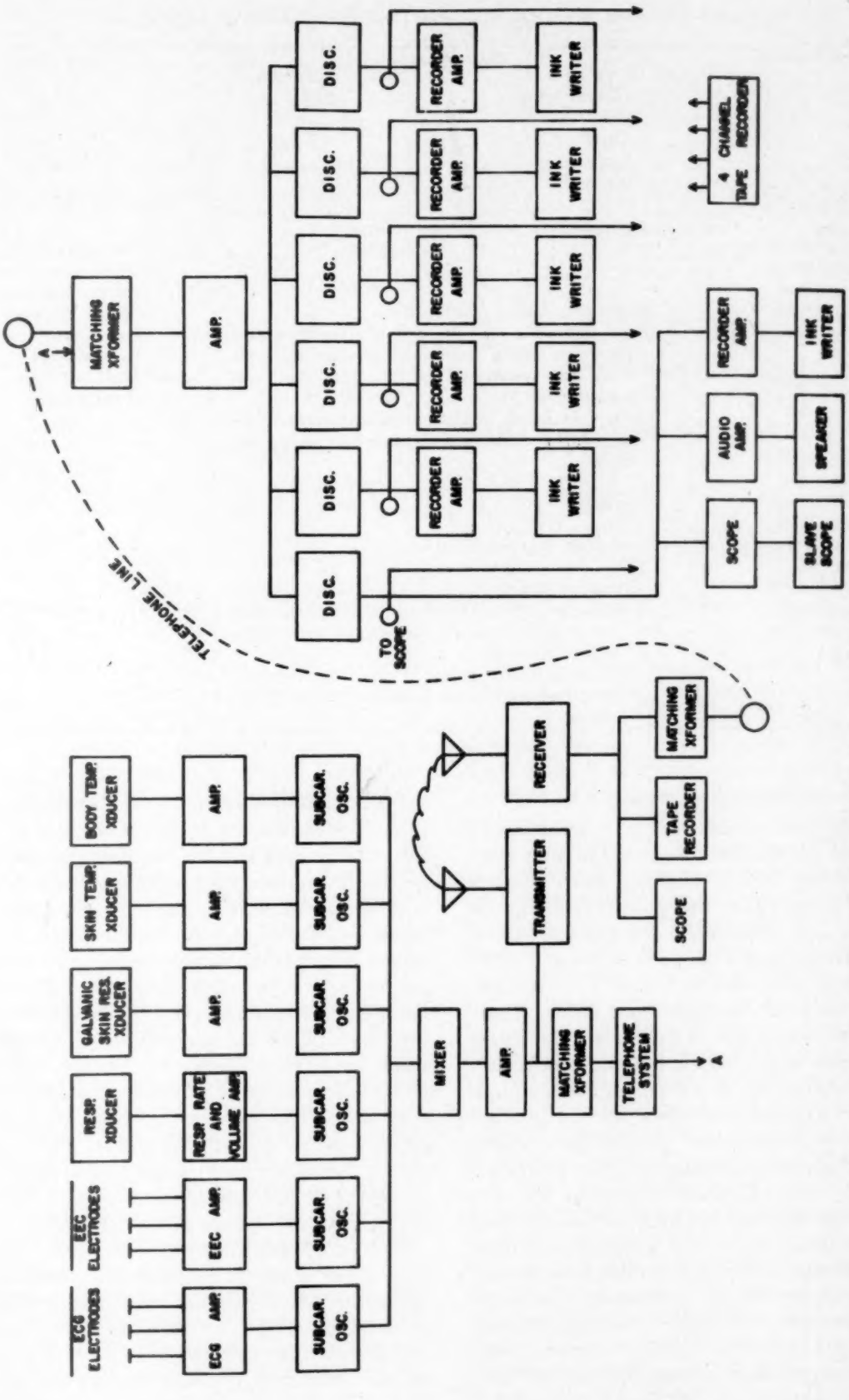
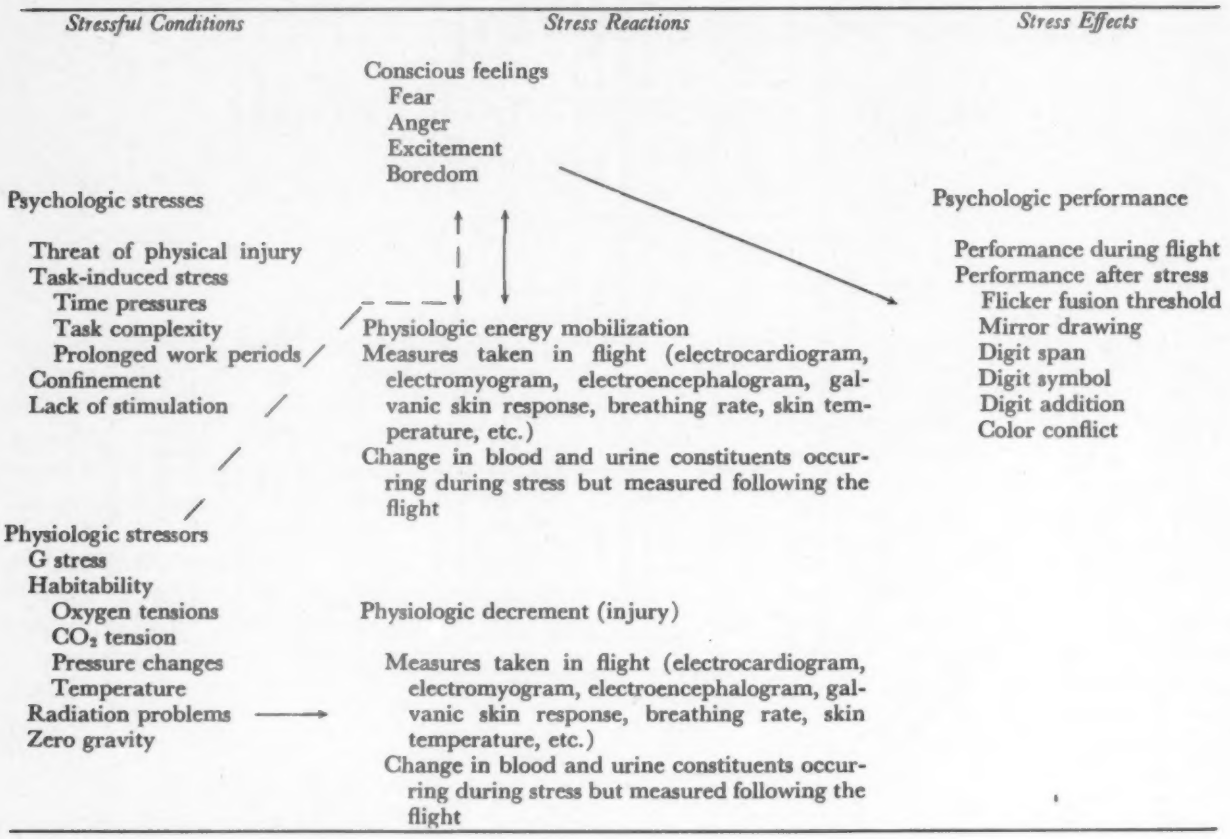


FIG. 1. Scheme for telemetering equipment for transmission and recording of data.

TABLE 1
Schematic Analysis of Stress Reactions and Their Effects on Pilot's Performance



Reactions to Stress

The equipment described has made possible the study of physiologic responses of man and animals during actual flights. Such studies have been directed at the problem of human psychologic and physiologic reactions to stress. The theoretical approach used in these studies of stress is schematized in Table 1. This approach divides the problem into three areas: the stressful conditions themselves; the emotional reaction of the person to these conditions; and the effects of his reactions on his performance. The stressful conditions can be divided into two broad categories: physiologic stressors and psychologic stressors. The *physiologic stressors* are those physical factors of the environment of the cockpit such as oxygen and carbon dioxide tension, and pressure and temperature changes of which the pilot may or may not be aware. These physiologic stressors generally produce their effects by direct action on the body and its functioning. For example, hypoxia may produce unconsciousness without psychologic awareness. *Psychologic stressors*, on the other hand, typified by the threat of physical injury, confinement, or the time pressures and complexity of the task required of the pilot, generally produce their effects by provoking an emotional reaction within the person. Such emotional reactions are accompanied by conscious feelings such as fear, anger, excitement or boredom, and by a physiologic mobilization of energy which generally results in increased heart rate and blood pressure, reduced gastric motility, etc. If the subject is aware that he is being affected by a physiologic stress, then it may also affect him in the same manner as a psychologic stress. For example, if the pilot is aware that his oxygen mask is not functioning properly, he may recognize a threat to physical energy and experience a reaction of fear.

Methods of Analyzing Stress Reactions: The first step is to analyze the stressful conditions to determine which stressors are of most significance in a given situation. Methods are then developed to rate or measure the severity of the stress. Where psychologic stresses are involved it is frequently possible to set up ratings of the

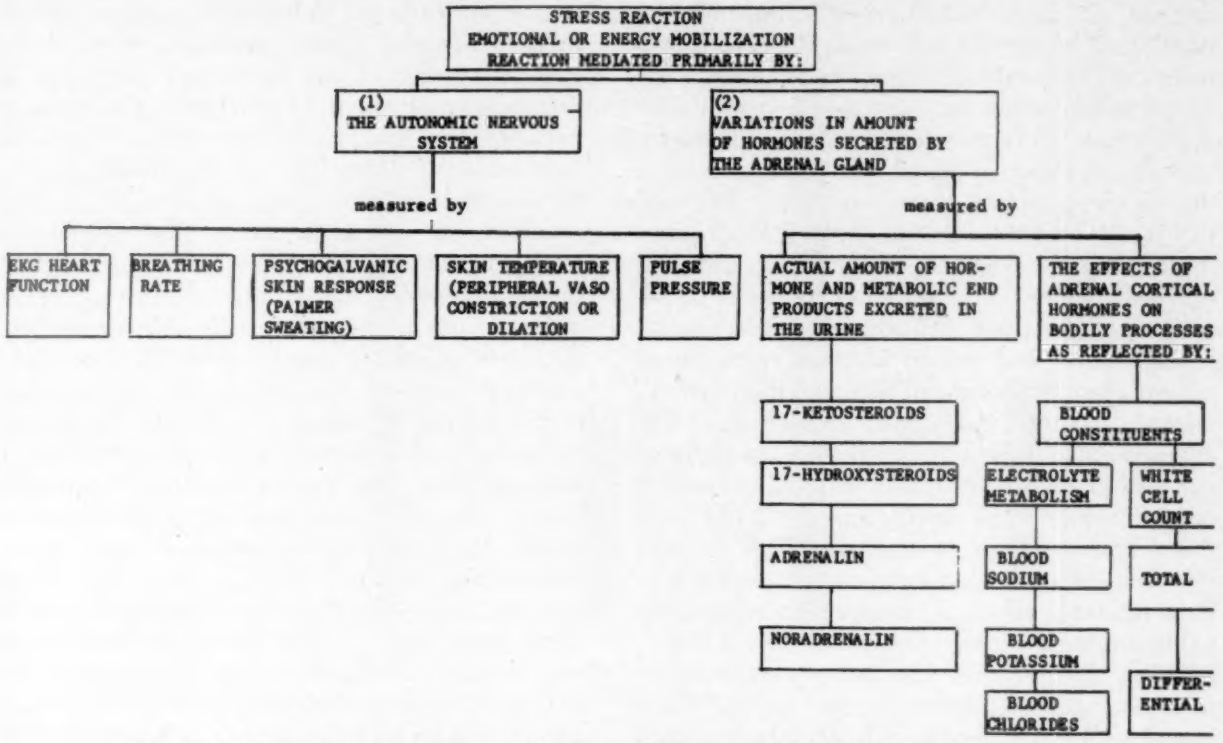


FIG. 2. Theoretical mechanisms underlying methods of measuring pilot's reaction to stress.

severity of stress encountered on particular flights. For example, routine training flights may have low levels of stress while operational flights in bad weather or with live ammunition may involve high levels of stress. Therefore, it is generally possible to rank the levels of stress involved in various flights and to compare the reactions of the pilot to each type of flight. In the case of physiologic stress it is frequently possible to make more direct and accurate measurements. For example, pressure changes and g levels in the aircraft may be measured and telemetered. Once a method of measuring or rating the severity of the stressful conditions has been developed attention is turned to the measurement of the pilot's reaction to stress. Two major types of measurements are available. Measurements of electrophysiologic responses may be made during flights and telemetered to the ground, or blood and urine samples may be taken before and after flights and the change of their constituents measured. Figure 2 illustrates the theoretical mechanism of these methods. The electrophysiologic measurements made during flight are primary responses mediated by autonomic nervous system activity. They give information on the emotional response and the physiologic status of the subject during the period of flight. The blood and urine measurements primarily reflect the activity of the adrenal cortex and medulla. These chemical effects are initiated during the period of high stress and persist for some time after the end of stress. Both types of measurements give information on the reactions of the subject to the stresses he has encountered.

Effects of Stress on Performance: If the stressful conditions are severe enough they lead via either an energy mobilization reaction or a physiologic decrement to an alteration in performance. Studies of performance under stress indicate that there is extreme variability in response to stressful conditions. On the one hand, people vary in their emotional response or the physiologic decrement produced by stressful conditions and, on the other, they vary in the amount a given emotional response or physiologic decrement will affect performance. Six major effects of stress-produced emotional responses may be noted: (1) The stress-produced energy mobilization improves performance of simple tasks and reduces performance of complex tasks. This results from the fact that simple tasks are primarily related to the level of energy expended upon them, while the performance of complex tasks is more related to previous learning and higher mental processes which may be upset or interfered with by high levels of energy mobili-

zation. (2) Large motions may be improved or unaffected by stress while small delicate movements will generally be disrupted by stress. (3) There is frequently an increase in nervousness and tremors which interfere with fine movement, and an increase in speed of reaction, with a decrease in accuracy of performance. The subject is more easily startled; he will react more rapidly but his reactions are generally diffused, not well defined, and therefore reduced in accuracy. (4) Attention to the critical factors for a given test is reduced by focusing attention on unimportant or irrelevant factors which are not related to the task being performed. For example, attention may be focused on the subject's own feelings or on an external source of danger rather than on the task at hand. (5) Stress causes people to be less flexible in their response. (6) Finally, subjects may regress in their behavior to simple more direct approaches to the problem. Since the pilot's task is highly complex and requires fine and accurate movement, complete attention to the task at hand and flexibility in meeting emergencies, it should be expected that the effect of stress-produced emotional reactions or physiologic decrement would be to reduce the efficiency of the pilot's performance.

Methods of Measuring Pilot's Performance During Stress: Two approaches are generally open for the measurement of the pilot's performance. (1) Performance of the pilot's mission may be measured. The problem is that success of the mission is generally a poor measure of pilot's performance since it is frequently highly dependent on a number of other factors such as weather and performance of the aircraft which are not related to the pilot's performance. (2) An alternate approach is to give special performance tests to the pilot. Since the pilot is usually fully occupied during the period of the flight itself, such tests must precede or immediately follow the actual period of stress. A number of psychologic tests which have been shown to be sensitive to the effects of stress are available for this purpose. The major problem here is that by the time it is possible to make such measurements the stress reactions have frequently disappeared.

Applications of Procedures: The equipment and procedures described herein are used for two purposes: first, to monitor the safety of hazardous operations, and second, to supplement laboratory stress studies with data on human reactions under the actual environmental conditions encountered in flight. The goal of the operational research on stress, like that of the laboratory programs of research on stress, is to determine the relation between the intensity of the stressor and the amount of reaction to stress (either energy mobilization or physiologic decrement) and to measure the extent to which the reaction to stress may affect performance. Monitoring the safety of operational flights requires accurate data on the relation between the physiologic measures which are part of the reaction to stress and their effect on the performance of the pilot. The desire is to detect in advance dangerous physiologic conditions which may promote a decrement in performance resulting in an accident. The three-part analysis of this problem appears to be an improvement over many of the approaches to stress used in the past. Frequently, studies on stress have considered two of these three phases. The results of such studies are frequently difficult to interpret because the experimenter who does not measure the physiologic reactions to stress often fails to demonstrate that his subjects were aware of or affected by the stressors which he applied. On the other hand, some investigators deal only with the physiologic reactions to stress. However, since a given amount of decrement or energy mobilization may produce differing amounts of decrement in performance, the significance of emotional decrement cannot be evaluated. It should be kept in mind that a certain level of energy mobilization is necessary for the proper performance of many tasks. Therefore, the existence of an emotional reaction does not necessarily indicate that the pilot's performance is adversely affected. The essential question is "Is the emotional reaction great enough to produce a decrement of performance?"

Monitoring Safety of Hazardous Flights

The hazards which confront man in flight are well known. Of particular importance are those factors which, because of man's limited sensory equipment, may incapacitate him without his awareness. An example of this type of hazard is the problem of hypoxia. Man has no sense organ to detect the lack of oxygen. Therefore, he may fall into a hypoxic state without being aware that he is in trouble. With the pilot already overloaded with instruments to watch, oxygen gauges and warning systems are only a partial answer to this problem. Where special hazards are expected, as in stratospheric

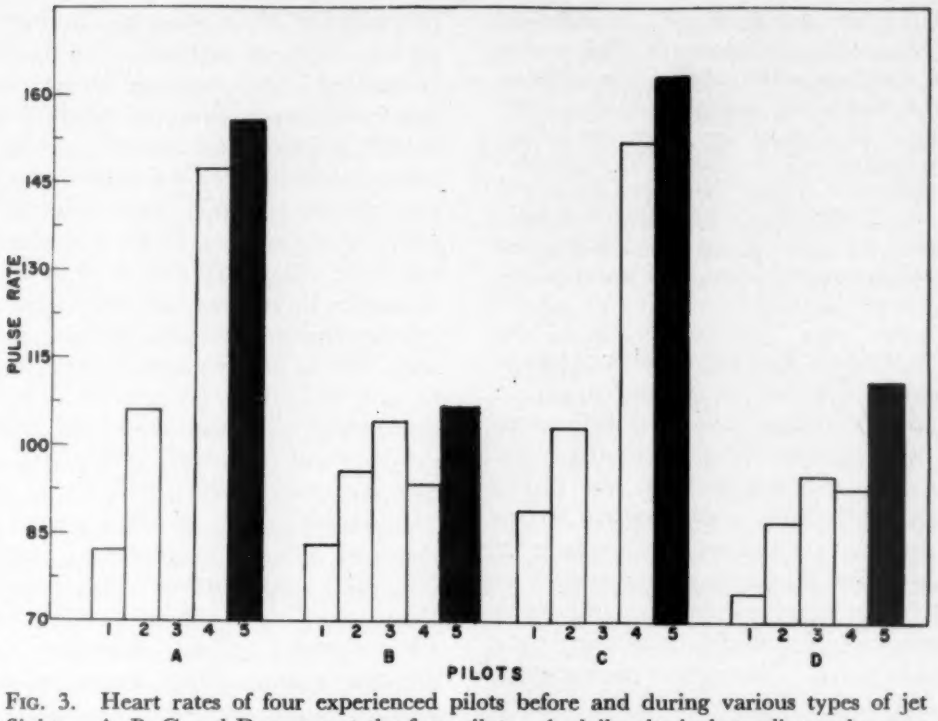


FIG. 3. Heart rates of four experienced pilots before and during various types of jet flights. A, B, C and D represent the four pilots. 1, daily physical-standing pulse rate. 2, immediately after flight. 3, captive flight. 4, average for air launch. 5, rate at launch point.

balloon ascents, telemetering equipment makes it possible to monitor such physiologic responses as heart rate, breathing rate and oximeter readings from the ground. This permits the flight surgeon to detect the first signs of trouble and take appropriate action. For this purpose, criteria for terminating stressful flights must be adopted.

The problem is to obtain sufficient information about the normal variation of such physiologic functions as heart rate and breathing rate to establish maximum safe levels to be permitted during the flight. Unfortunately, experience has indicated that the usual concept of normality does not apply in flight operations. For example, when responsibility for monitoring the safety of the stratolab balloon ascents was first assigned, a group of experts in medicine and physiology were brought together to determine the maximum safe levels of heart rate, respiration and other physiologic measurements. As a result of this conference, maximum acceptable heart rate was tentatively set at 130 per minute and the maximum safe rate of inspiration respiration was tentatively set at 30 per minute. However, these criteria were soon abandoned. The first operation in which there was an attempt to apply these criteria was a balloon ascent in an open basket through a thunder cloud. Psychologically, this ascent was highly stressful since the turbulence and electrical build-up within the cloud presented a definite threat to the operation's safety. Electrocardiographic and respiration rate recordings from one member of the two-man crew indicated that his heart rate was 180 and his respiration rate 70 per minute before the gondola left the ground. These high rates were maintained throughout the early part of this particular operation. Thus, it was impossible to enforce the original criteria.

Another problem encountered in monitoring the safety of an operation is illustrated by the data in Figure 3. This illustration gives the heart rates collected from four experienced pilots as part of the study of stress in operational flying. Measurements of heart rate were made both on the ground and during various types of jet flights. The left-hand bar gives the average heart rate recorded during daily physical examinations. These are standing pulse rates taken on the ground. The next bar indicates the average pulse rate taken immediately after return from a jet mission while the pilot was still seated in the cockpit. The third bar indicates the average pulse rate during routine training flights involving no particular stress. The fourth and fifth bars give the average rate during stressful live firing runs and the heart rate at the point of maximum stress in this firing run, respectively. The point of particular

interest is that while the heart rate of all pilots increases to some extent during the flight when compared to standing pulse rate on the ground, the pulse rate of two of the pilots shows a very much larger increase than that of the other two. This large individual difference in reaction to an essentially similar condition makes the application of a set criteria for terminating flights impossible. Rather, criteria specific to the pilot must be formulated on the basis of a thorough preliminary study of the responses of each subject.

Underlying the facts that the usual concepts of normal physiologic functions do not apply in the aircraft, and that large individual differences in reaction occur, is the effect of emotional responses obscuring the responses to the physiologic stressors. Hypoxia may produce an increase in breathing rate and an increase in heart rate. However, emotional responses appear to have a much larger effect on breathing and heart rate and therefore are likely to obscure any effects due to hypoxia. This is true even though the measurements are taken on highly experienced successful flyers who would be expected to show a minimum of emotional reactions during flight. It is also important to be aware that despite these large changes in physiologic response, the pilots were able to perform this mission with no apparent decrease in efficiency.

Operational Research

There are two basic approaches to the problem of determining the effects of flight on the living organism.

One approach might be termed a laboratory experimental method. In this procedure data about the environment encountered in flight are collected by instruments on the ground or in special vehicles such as high altitude balloons. On the basis of these data this environment can be simulated in the laboratory for biologic studies.

Another, the operational approach, is to place an organism in the plane and study its reactions under actual flight conditions. Obviously these two approaches are not mutually exclusive alternatives. Since each has unique advantages both should be and are being carried on at once. The primary advantage of laboratory procedures is the precise control that can be exercised over the environment itself, and over the physiologic and psychologic measurements of the subject's reaction to this environment. Precise control is not possible in the operational approach; however, there are important advantages to this procedure. Most obvious is the fact that not all the effects of flight may be simulated in the laboratory. For example, travel in or on the border of space involves weightlessness which cannot be simulated completely in the laboratory. Moreover, in the laboratory it is usually possible to simulate only one or two components of the total flight environment at any one time. An organism may be able to adjust to partial simulation but break down under the impact of the additional stresses present in the actual flight environment. Nor, finally, can we be sure that all the hazards of such new areas as space flight have been identified. Only survival in space will demonstrate that this new frontier has been conquered.

For the purpose of in-flight research, man is the most valuable subject since it is to him that we must apply data from any experiment. However, when, as in space flight, the hazards are too poorly understood to warrant risking the life of a human being, lower animals serve as subjects. The man or animal and his compartment serve essentially as a biologic instrument on which to record the effects of the environment to be studied. The important features of this equipment, as with any mechanical or electronic instrument are sensitivity, reliability and durability. In addition, because of the limitations of the vehicle, considerations in size, shape and weight are also important. If the instrument is to be used in or near the borders of space, it will have to be completely self-contained, requiring no outside source of energy. Like all instruments this biologic measuring device requires calibration. In order to obtain a maximum of information from the physiologic and psychologic measures available, control data must be collected under normal, non-stressful conditions and under simulated stress of various types in order that the normal and the stress response levels of these measures for each subject will be known in advance. This involves a series of preflight tests under non-stress conditions and during exposure to such stressors as increased g, reduced pressure, reduced oxygen tension and variations in temperature. Typical patterns of reaction under these conditions must be determined. Once determined it is then possible to contrast the telemetered data with these control measurements. These preflight control data are particularly important in the case of animals in space vehicles since, at least at first, it will not be possible to return the animal to the ground. In such a case the value of the

telemetered data is almost entirely dependent upon the adequacy with which the animal's responses have been studied prior to the actual space flight. During the actual operation itself the basic problem is to record the condition of man or animal at all times and to determine whether it is performing up to the expected level. The cause of unexpected patterns of physiologic activity or of a performance decrement must be determined against the background of information previously obtained on the characteristic response of the organism.

Summary

Modern technology has provided means for transmitting to remote locations nearly all physiologic responses which involve external electrical, mechanical or thermal changes. These developments have made it possible to make precise physiologic measurements under operational conditions of the type that only a short time ago were limited to the laboratory. Since transmission of these responses is possible, the pilot's physiologic reactions may be monitored from the ground in order to protect him from environmental hazards to which he is insensitive. A major problem which arises in connection with this procedure is that emotional responses obscure physiologic reactions, resulting in reactions beyond what are normally considered safe and producing large individual differences in reactions. To overcome these problems careful studies of each subject to be monitored must be made prior to the actual experimental flight. Telemetering also permits experimental study of stratosphere and space flights. Here again, control data are essential since in many cases it will not be possible to return experimental animals to the earth and therefore all information on their status in space must be gathered by comparing telemetered physiologic recordings with control data collected on the ground.

Vectorcardiography in Aerospace Flight

Applications and Rationale*

MAJ. GEORGE B. SMITH, JR., MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

VECTORCARDIOGRAPHY promises to be an increasingly important tool in evaluating the cardiovascular status of the pilot and in monitoring cardiovascular function during aerospace flight. The problem of assessing the cardiovascular status of the asymptomatic healthy-appearing American man is well known.

Utilizing vectorcardiographic principles detailed in this report, it is possible, in many instances, to separate electrocardiograms consistent with infarction that are in reality due to electrical field or anatomic factors from true examples of infarction. The importance of this distinction in the man to be in primary control of high performance aircraft is obvious. Statistical analysis of change in QRS amplitude in routine electrocardiograms has demonstrated a correlation of amplitude with increasing age.[1] This important point means the intensity of the electrical field generated by the heart diminishes with age and that accurate quantitive three-dimensional analysis as provided by the quantitive vectorcardiogram should provide an index to aging of the heart.

Evaluating cardiovascular function during flight necessitates an electrical approach. Cardiac output cannot be measured by dye dilution curves, catheterization studies or a host of other common laboratory procedures. The order of ventricular excitation with the cone concept suggests that some index of cardiac dynamics can be studied by three-dimensional electrical analysis. Study of the electrocardiogram in different phases of respiration has demonstrated changes in QRS amplitude which seem to be related to physiologic changes in filling of the right and left ventricles.[2]

Aerospace flight requires that the participant be exposed to increased gravitational force (g) and in certain flights, the weightless state. These alterations in g force result in cardiac displacement. An accurate evaluation of S-T segment and T wave changes requires a three-dimensional comparison to QRS events to prevent misinterpretation of simple positional changes. For these reasons recording from three vectorcardiographic leads is desirable for monitoring purposes. The methods outlined in this report have been successfully used in human subjects utilizing the F-100 aircraft and flying parabolas that induced increased g load as well as transitory periods of weightlessness. An adaptation of the method was attempted with somewhat less success in the small primate studies carried out in missile shots.

The purpose of this report will be to highlight some basic principles of vectorcardiography, not commonly appreciated, that influence its applicability in aviation. A fundamental knowledge of the relationship of the vectorcardiogram to cardiac events and to the routine electrocardiogram is essential in assessing each tool's proper place in aviation cardiology. A subsequent report will detail its application to the problem of silent infarction.[3]

Vectorcardiography has done a great deal to dispel the maze of misconceptions in and complexity of electrocardiography. It has provided a more scientific basis for three-dimensional analysis of the electrical events of the heart. In so doing it has destroyed the mystery surrounding pattern electrocardiography with its infinite number of variations, recorded by innumerable electrocardiographic leads. By adding additional parameters for three-dimensional vectorial analysis, by providing a more satisfactory undistorted lead system for the human body and by providing a whole new concept in instrumentation, vectorcardiography has provided a more sophisticated

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

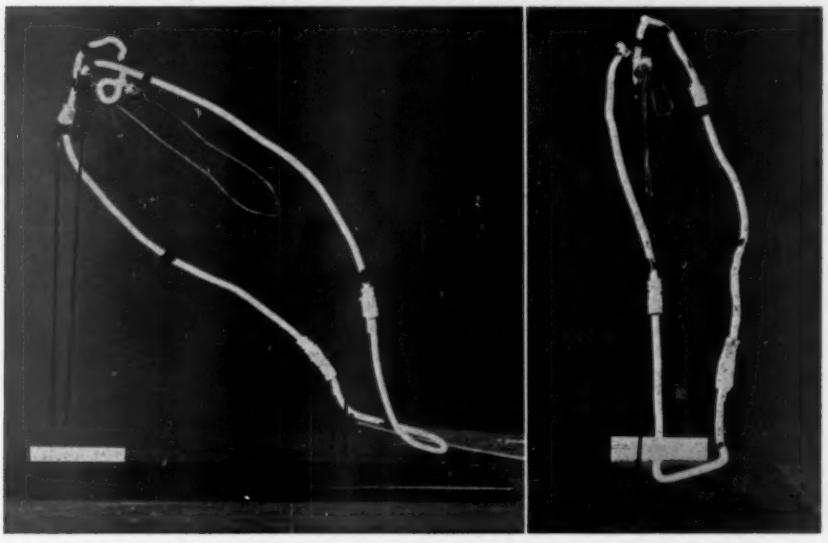


FIG. 1. *At the left* is a frontal view of a three-dimensional vectorcardiographic model. The smallest loop in the center is the P loop; the larger loop in the center is the T loop; the largest loop is the QRS loop. Each black time marker on the QRS loop represents 0.01 second. *At the right* is the left sagittal view of the same model. The QRS loop moves in the anterior direction first. The terminal portion of the QRS loop continues directly into the T loop without closures and is analogous to S-T segment displacement on the electrocardiogram. This vectorcardiogram is from an athlete training for the Pentathlon events of the Olympics. Large T loops are frequently seen in the athlete.

approach to the study of the electrical events of the heart.

Electrophysiologic Basis of Vectorcardiography

Since the heart is a three-dimensional organ, not a strip of muscle, the electrical forces created by it have three dimensions. Although many different regions of the heart may be electrically active at any one time their resultant effect can be depicted as a single vector (dipole vector). As new regions of the heart become electrically active the orientation of the dipole vector changes. If the electrical activity is measured from sites remote from the heart the successive dipole vectors behave as if they acted on a single point of origin. This is particularly true for ventricular excitation. As the orientation of the dipole vector changes, its rotating tip describes a three-dimensional arc, curve or loop. When the heart is at rest, no significant forces are measured and the dipole vector, consequently, has a magnitude of zero. During atrial excitation a force is created, and as the dipole vector changes its orientation its tip describes a spatial pathway or loop, called the P loop. At the completion of atrial excitation there is again little or no measurable electrical force and the magnitude of the dipole vector is zero. Similarly, ventricular excitation and recovery create a series of changing dipole vectors which may be represented respectively by the QRS and T loop of the vectorcardiogram (Fig. 1).

The heart normally undergoes excitation and recovery in a systematic fashion, not in a disorganized, random sequence. Failure to appreciate the orderly sequence of ventricular excitation has led to considerable folklore concerning the electrocardiographic diagnosis of septal myocardial infarction, septal vectors and a host of other unsound concepts. The normal sequence of ventricular excitation provides the basis for meaningful vector analysis. Excitation begins with the formation of two confluent conical wave fronts at the endocardial surface of the right and left ventricles. The wave fronts move outward and are dissipated at the epicardial surface. The systematic disintegration of the conical wave fronts is in fact responsible for the systematic sequential orientation of the successive dipole vectors.

Ventricular Excitation: An analysis of excitation through a simple wedge section of the left ventricle demonstrates the principle of vector analysis (Fig. 2). As the wave front migrates outward its area becomes progressively smaller. The resultant vector decreases in magnitude as

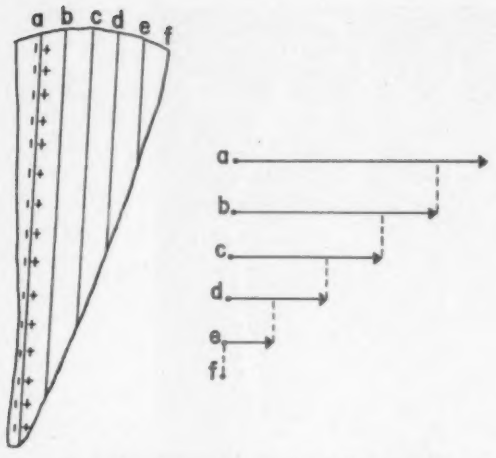


FIG. 2. A wedge segment of the left ventricle with a wave front of excitation moving from the endocardial out to the epicardial surface. See text.

the area of the wave front diminishes. The resultant force in a nearly flat wave front is equal to the area (S) times the density of charge (ϕ) or ϕS. Assuming that the density of charge (ϕ) is not significantly altered, as the wave front moves outward, the change in the resultant vector magnitude is directly related to the changing areas (S) of the wave front. With these assumptions, in this elementary example, the sum of the differences in vector magnitude at time intervals *a* through *f* is equal to the magnitude of the resultant vector acting at time interval *a* or

$$(a - b) + (b - c) + (c - d) + (d - e) + (e - f) = a.$$

It follows that the area (S) which completed excitation between time interval *a* and *b* is directly related to the difference in magnitude of resultant vector *a* and *b*.

Determining the difference in magnitude of the vectors by simple subtraction to evaluate the change in wave front area (S) is quite satisfactory for disintegration of a flat wave front. Ventricular excitation, however, results in disintegration of three-dimensional wave fronts. Addition and subtraction of vectors with different spatial orientation must be accomplished by accepted vector principles using the parallelogram method or polygon and polyhedron analysis. Given vectors *a* and *b* acting simultaneously at a common point of origin at a time interval of 0.01 second, their resultant, the diagonal of a parallelogram, is the manifest 0.01 second vector (Fig. 3). It follows that the distance between the tips of the 0.01 second vector and vector *b* is equal to the magnitude of vector *a* (opposite sides of a parallelogram).

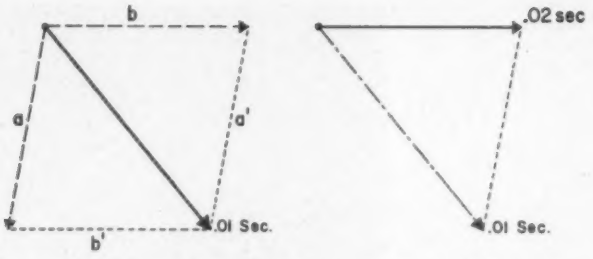


FIG. 3. The parallelogram theorem is the basis for vector analysis of forces acting on a common point but not parallel to each other. It may be extended into polygons or polyhedrons. The latter is analogous in a geometric sense to the three-dimensional vectorcardiogram. See text.

If the force represented by vector *a* is abolished at the 0.02 second time interval, vector *b* becomes the manifest 0.02 second vector. If the magnitude and spatial orientation of the 0.01 second and 0.02 second vectors are known, the magnitude and orientation of vector *a* can be determined by simply constructing a line between the vector tips of the 0.01 and 0.02 second vectors. It is quite apparent that vector *a* cannot be determined by simple subtraction of the magnitude of the 0.02 second vector from the 0.01 second vector. To determine the arithmetic sum of vector *a* and *b* (not vector resultant) the distance between the tips of the 0.01 and 0.02 second vectors is added to the length of vector *b* acting at 0.02 second. Only in this manner can an arithmetic sum of the vector forces involved be determined.

As the three-dimensional cone of activity created by ventricular excitation disintegrates the dipole or manifest vector changes its spatial orientation and magnitude. The segment of the QRS loop between the tips of resultant vectors at two different time intervals is related to the difference in size and orientation of the wave front for the two points in time (Fig. 4). The details of ventricular excitation are sufficiently well documented and will not be discussed further here; let it suffice to say that the loop itself provides a distinctly different measurement from those obtained from the changing magnitude of the dipole vector (instantaneous vector).[4–6]

Measurement of Magnitude of QRS Vectors: It has been suggested previously that various portions of the QRS loop are directly related to the size of the endocardial cone of excitation and thus to the ventricular volume.[4] If the relative area (S) of a conical segment is known as

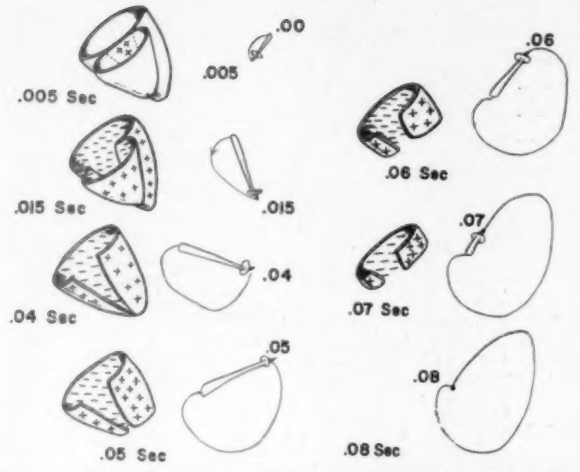


FIG. 4. Ventricular excitation chiefly involves the disintegration of two conical wave fronts. The changing dipole vector resulting from progressive disintegration creates a three-dimensional pathway or polyhedron (vectorcardiogram).

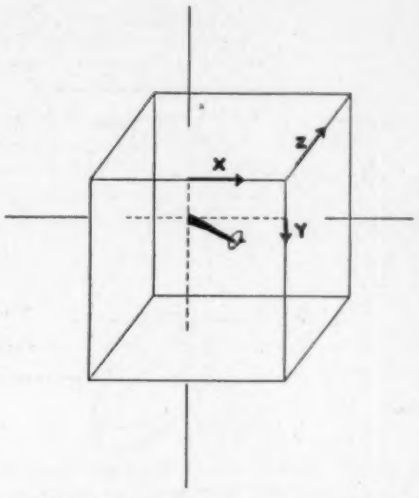


FIG. 5. Any spatial vector may be resolved into three mutually perpendicular components depicted here as X, Y and Z.

well as its relative duration of action a true electrical force per unit of time measurement can be obtained. Time units applied to magnitude of the dipole vector are another measurement and can only represent the resultant voltage (like the diagonal of the parallelogram) through time. In the past the parameter offered by the loop has been ignored, chiefly because the emphasis of vectorcardiography was placed upon the instantaneous vectors alone. This was a natural outgrowth of the historic development of vectorcardiography which followed years after electrocardiography was known. Electrocardiograms graph along a time coordinate the projection of instantaneous spatial vectors.

By constructing a three-dimensional vectorcardiogram with instantaneous vectors acting on a common point of origin one admits to the validity of its geometric analysis. That which is "sauce" to the instantaneous spatial vectors is "sauce" to the loop itself. By geometric analysis it is clear that the segment of the loop between any two successive spatial vectors is one side of a parallelogram and is the vector expression of the difference between the two successive spatial vectors. It has also been proposed that measurement of the magnitudes of successive spatial vectors and the angle between them as viewed in two planes would be of great value.[7] Obviously, any measurement of this nature is related to the two sides of a triangle (the two instantaneous vectors and the angle between them). This is not dissimilar from measuring the segment of the loop, but is more complicated. By the elementary geometric theorem of "side angle side" it is known that the third side of the triangle (the loop segment) can be determined. The importance of the angle between successive instantaneous spatial vectors is recognized and is related to simple vector analysis using the parallelogram as described.[8] The use of the additional parameter offered by the spatial vectorcardiographic loop provides an opportunity for new research relative to the cardiovascular system. How useful it might be in terms of evaluating electrical power, hypertrophy, ventricular volume or the loss of electrically generating muscle awaits further investigation.

Recording the Vectorcardiogram

Projections of Spatial Vector Loop: Conventional vectorcardiograms display the three-dimensional loops as if they were projected on a two-dimensional plane. It is customary to use a frontal plane projection (as if one were facing the subject), a sagittal plane (profile view) and a transverse plane (transverse cross section through the chest). Two such perpendicular planes, e.g., frontal and sagittal, recorded simultaneously, permit a three-dimensional analysis of the spatial forces. Commonly, a cathode ray oscilloscope with suitable amplifiers is used for recording purposes. Such an instrument provides a better frequency response than those of the direct writing instruments used in electrocardiography.

Each of the successive instantaneous spatial vectors have components in three mutually

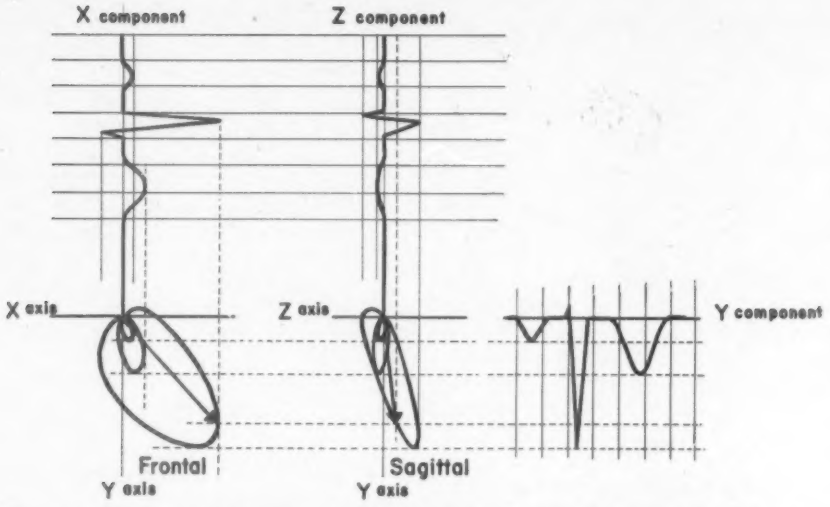


FIG. 6. The vectorcardiogram is created by three mutually perpendicular components of the electrical activity of the heart. The components may be graphed in a linear fashion similar to an electrocardiogram. See text.

perpendicular (orthogonal) axes. Each spatial vector has a horizontal component (X), a vertical component (Y) and an anterior-posterior component (Z) as shown in Figure 5. By plotting the X component of the successive instantaneous spatial vectors along a linear time base, a coordinate graph of the X components is formed. This will appear similar to lead I of the electrocardiogram which supposedly measures the changing magnitude of the forces of the electrical cycle in a left-to-right direction. In a similar fashion the Y component of the successive instantaneous vectors may be plotted as a coordinate graph (similar in appearance to lead aVF) and the Z components may be plotted as a coordinate graph (similar in appearance to lead V_2).

Component Leads: By utilizing the cathode ray oscilloscope and introducing any two component values in a continuous fashion to one beam a view of the three-dimensional vectorcardiogram is seen as it is projected on one plane. With a continuous input of the X components into the horizontal axis of the oscilloscope and simultaneously utilizing the Y component measurements for an input to the vertical axis of the oscilloscope, the frontal plane is formed (Fig. 6). Similarly, an input of the Z component values and the Y component values results in a sagittal plane, or the input of the X component values simultaneously with the Z component values will record the transverse plane presentation of the electrical forces. It is obvious that the inputs to the perpendicular deflection plates of the oscilloscope must be accurate representations of the X, Y and Z components of the changing spatial vector or the recorded loops will not be a true representation of the spatial pathway created by the electrical forces of the heart. To obtain true representations of the X, Y and Z components it is necessary to use a system of three leads from the body surface that are truly mutually perpendicular. To further prevent distortion, the leads must have the same relative sensitivity or be accurately equilibrated. Attempts to obtain an accurate lead system have resulted in considerable controversy relative to electrode placement.

Electrocardiographic leads are coordinate graphs of the electrical events of the heart. In this regard they are similar to a graph of the X, Y and Z components on a linear time base. The configuration of the electrocardiographic complexes in any lead is largely dependent upon the lead's electrical axis as a coordinate and the projection of the electrical forces of the heart on it. This relationship permits construction of electrocardiographic complexes for any lead from the vectorcardiogram when the coordinate axis of the lead is known. Analysis of this type neither proves nor disproves the validity of the vectorcardiographic system used.

Use of the conventional leads, I, II and III or leads derived from this system will not provide true X, Y and Z inputs. The Einthoven triangle is a simplification and an assumption, not a fact. The limb leads do not form an electrically equilateral triangle. The triangle

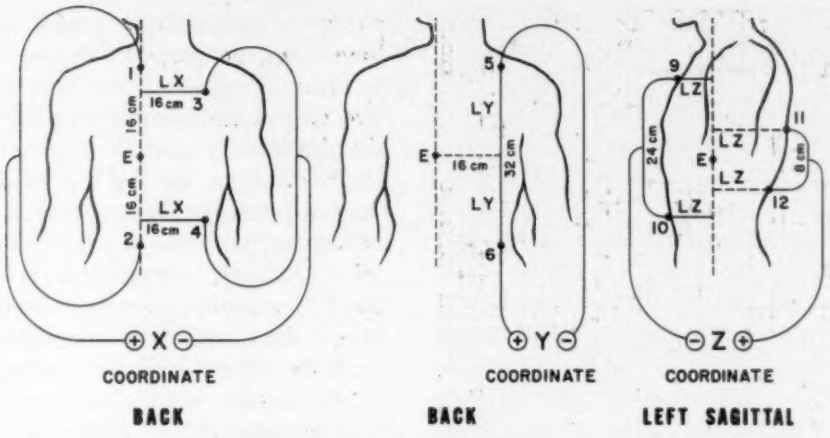


FIG. 7. The electrically balanced bipolar vectorcardiographic reference system utilizes ten electrodes. The E point is over the center of the left ventricle (usually 3 to 4 cm. to the left of the midline). In the average adult man their placement is as follows: *X Lead:* positive electrodes 1 and 2 are placed 16 cm. above and below E point on the back. Negative electrodes 3 and 4 are placed 16 cm. to the right and 12 cm. above and below E point on the back. *Y Lead:* negative electrode 5 is placed 16 cm. to the right and 16 cm. above the E point on the back. Positive electrode 6 is placed 16 cm. to the right and 16 cm. below the E point on the back. *Z Lead:* negative electrodes 9 and 10 are placed 16 cm. to the right and 12 cm. above and below E point on the anterior thorax. Positive electrodes 11 and 12 are placed 16 cm. to the right and 4 cm. above and below E point on the back.

that is formed may depart as much as 35 degrees from the true frontal plane. Combination of the conventional electrocardiographic leads (to form vector loops) cannot generate information not already present in the electrocardiogram and thus, these leads are unsatisfactory for vectorcardiography. The addition of an electrode on the back to form the tetrahedron reference system does not alter this fact. The construction of schematic vector loops from routine electrocardiograms provides little more than exercise for the electrocardiographer to demonstrate the assumed relationship of the common electrocardiographic leads to each other.

In the past few years a great deal has been learned about the body as a volume conductor and about its influence on the potentials generated by the heart. Using this knowledge and some newer technics of study it is possible to devise near perfect combinations of leads to portray the true electrical phenomena of the heart.

Reference System for Recording and Measuring Component Leads: A system of electrically balanced bipolar leads to measure the X, Y and Z components as used by us, and electrode placement for the average adult is depicted in Figure 7. The reference system is unique in that it is based on physical measurement of surface potential from the human torso; thus, no assumptions are necessary about the body as a volume conductor. The influence on recorded potentials of distance and resistance at various surface points was measured to determine the placement of electrodes which would produce undistorted leads for vectorcardiography. The comparative vectorgram technic was used for this study. This method permits comparison of similarity of leads with a high degree of accuracy. This technic makes it possible to determine also how far an electrode should be from the heart to actually represent the electrical activity as a resultant vector. Many reference systems currently in vogue place electrodes too near the heart for true representation of a resultant vector. The details of making these measurements, their use in constructing an electrically balanced lead system, as well as a method of analyzing other systems currently in use, have been published elsewhere.[9–11]

It has been found relatively easy to measure the vertical component of the electrical forces of the heart with two electrodes on the trunk. In the system illustrated, the X and Z leads are each composed of four electrodes. This is necessary to cancel components in other than the desired direction.

The method is simple and accurate. It does

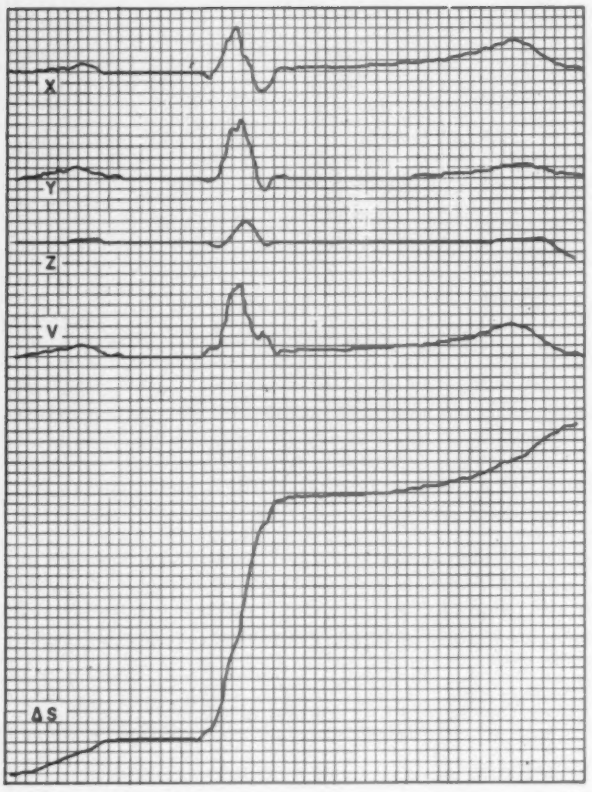


FIG. 8. The linear vectorcardiogram displays the X, Y and Z components along a linear time base. The upper three graphs represent these. The magnitude of the instantaneous vectors is represented on the fourth graph. The cumulative arc swept out for the P, QRS and T loops is plotted against time in the lowest graph.

not require complicated balancing of electrical circuits and the electrodes are sufficiently remote from the heart to measure the electrical activity of the heart as a dipole. Using the same methods employed to devise this particular reference system, it is an easy task to devise an individualized reference system for each patient. No claim is made that this is the only possible arrangement of electrodes; however, its simplicity and accuracy appear to achieve a prime objective of vectorcardiography, namely, a simple method of obtaining relatively undistorted representations of the electrical forces of the heart.

The Linear Vectorcardiogram: It is a simple matter to graph the X, Y and Z components of the vectorcardiogram along a time base just as is done routinely in electrocardiography. From these components, simple calculations make it possible to calculate the magnitude of the changing dipole vector throughout the cardiac cycle and graph it against a linear time base. The cumulative length of the P, QRS, and T loops (i.e., the distance traveled by the tip of the spatial vector) may also be calculated and plotted along a linear time base. Simple formulas have been developed for these calculations.

Thus, along a common base representing time, five coordinate graphs may be used to present simultaneously and in a linear fashion all the basic data in the vectorcardiogram (Fig. 8). Such a presentation has been called the "linear vectorcardiogram."[12] The information contained in such a graph cannot be obtained from the conventional electrocardiogram or from any other distorted combination of electrical leads. By presenting the vectorcardiographic data in a linear fashion two of the major criticisms of vectorcardiography have been circumvented, i.e., that the vectorcardiogram does not demonstrate rate or rhythm and that the duration of isoelectric periods cannot be measured.

Interpretation and Application of the Vectorcardiogram

As is often the case in any newly developed diagnostic tool, overly enthusiastic interpretations of data are frequently obtained. Conversely, there are unduly pessimistic interpretations by those using the method merely to obtain minimum information previously available by older diagnostic methods. A new tool should be evaluated by utilizing the new parameters it makes available. Minor variations in the contour of the QRS loop which are sometimes called "areas of avoidance" are often nothing more than the notching seen in the QRS complex of the routine electrocardiogram and at present are no more useful in clinical application. It is doubtful that the currently used criteria of interpretation in vectorcardiography ever enable diagnosis of infarctions that cannot be detected by the routine electrocardiogram. This may not always be the case as more is learned about the direction, length and speed of inscription of the QRS loop.

By taking advantage of the electrically balanced leads it is possible to demonstrate that a number of borderline routine electrocardiograms present apparent abnormalities because the routine electrocardiographic leads are electrically distorted by the individual characteristics of the body as a volume conductor. The best example of this is the electrocardiogram with a significant Q_2 Q_3 Q_{aVF} pattern. It is often impossible to be certain from the electrocardiogram whether or not this means that electrical forces are truly directed away from a muscle area on the inferior wall of the heart for a significant period of time. The undis-

torted vectorcardiogram demonstrates that many such electrocardiograms are created by lead distortion and in actuality the spatial forces are not significantly directed away from an area of muscle. The vectorcardiogram utilizing leads I and aVF for the X and Y components cannot be employed for this purpose and will give no more information than the routine electrocardiogram.

Certain criticism of vectorcardiograms is not warranted. Duration of the QRS complex in the vectorcardiogram is measurable with at least as great an accuracy as in the electrocardiogram. The end of the QRS complex and the beginning of the S-T segment in lead V_2, for example, is strictly arbitrary. Visualization of central detail of the vectorcardiogram can be achieved if enlargement of the image is done electronically, rather than photographically. The use of the Polaroid-Land® process for recording vectorcardiograms produces permanent records almost immediately which surpass the quality of recording on 35 mm. film. Intensity modulation of the oscilloscope beam aids in preventing a center "burn out" effect. The problems of recording rate or arrhythmia with the vectorcardiogram can be circumvented by high speed records of the components or by the "linear vectorcardiogram."

One of the newer approaches to recording electrocardiograms and vectorcardiograms is the use of wide magnetic tape and the simultaneous recording of several channels. These recordings can be played back at will and signals from the tape recordings can be reproduced by oscilloscopes or direct writing instruments or may be introduced into analog computers to perform desired computations. During flight the vectorcardiographic leads may be telemetered, received and recorded on magnetic tape. From the tapes vectorcardiograms or component leads against a linear time base may be obtained. The telemetered signals can also be monitored during flight by simultaneous display on the oscilloscope either as linear graphs, as vector loops or as both.

Summary

At present, it can be stated with certainty that the vectorcardiogram offers three distinct advantages over the conventional electrocardiogram:

1. It enables relatively undistorted representation of the electrical forces of the heart. (The validity of this statement depends on the reference system used.) Thus, the true magnitude and direction of the spatial vectors are available.

2. The loop or spatial pathway described by the vectorcardiogram provides a measurement that is not available in the routine electrocardiogram. This may be plotted along a time base as in the linear vectorcardiogram.

3. The use of a cathode ray oscilloscope rather than a direct writing instrument allows greater accuracy in presentation of rapid or minute changes in electrical forces.

The applications of vectorcardiography in assessing the pilot's cardiovascular system and in monitoring cardiovascular functions during flight are discussed. For fundamental reasons outlined in the report this technic promises to have even wider applications to future studies of cardiology in aviation.

References

1. Hiss, R. G. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. x. Normal values. *Am. J. Cardiol.*, 6: 200, 1960.
2. Lamb, L. E. Electrocardiographic changes in respiration and left and right ventricular stroke volume. *Am. Heart J.*, 54: 342, 1957.
3. Smith, G. B., Jr. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. ix. Myocardial infarction. *Am. J. Cardiol.*, 6: 190, 1960.
4. Lamb, L. E. Fundamentals of Electrocardiography and Vectorcardiography, p. 1. Springfield Ill., 1957. Charles C Thomas.
5. Scher, A. M., Young, A. C., Malmgren, A. L. and Paton, R. R. Spread of electrical activity through the wall of the ventricle. *Circulation*, 1: 539, 1953.
6. Wilson, F. N., Rosenbaum, F. F. and Johnston, F. D. Interpretation of the ventricular complex of the electrocardiogram. In: Advances in Internal Medicine, vol. 2, p. 1. New York, 1947. Interscience Publishers, Inc.
7. Abildskov, J. A., Ingerson, W. E. and Hisey, B. L. A linear time scale for spatial vectorcardiographic data. *Circulation*, 14: 556, 1956.
8. Lamb, L. E., Grosgurin, J. R. and Duchosal, P. W. Vectorcardiographic studies of ventricular hypertrophy. *Cardiologia*, 28: 65, 1956.
9. Smith, G. B., Jr. and Lamb, L. E. The comparative vectorgram, a simple method for analysis of lead similarity. *Am. J. M. Sc.*, 234: 434, 1959.
10. Lamb L. E. and Smith, G. B., Jr. A study of the human torso as a volume conductor by comparative vectorgram analysis—the dR factor. *Am. J. M. Sc.*, 237: 612, 1959.
11. Lamb, L. E. and Smith, G. B., Jr. An electrically balanced bipolar vectorcardiographic system: lead analysis and lead synthesis using the dR factor. *Am. J. M. Sc.*, 237: 759, 1959.
12. Lamb, L. E. The linear vectorcardiogram. *Am. J. Cardiol.*, 3: 766, 1959.

An Electrocardiographic Study of 17,000 Fit, Young Royal Canadian Air Force Aircrew Applicants*

GEORGE W. MANNING, M.D., F.A.C.C.

London, Ontario, Canada

SINCE THE selection of personnel for aircrew training was of vital importance at the beginning of World War II, the Royal Canadian Air Force Clinical Investigation Unit undertook a number of selection studies, one of which was to assess the value of the electrocardiogram in the medical selection of aircrew trainees.[1-3] An abnormal electrocardiogram did not preclude aircrew training at that time and it soon became apparent that no specific features of the electrocardiogram bore any relation to failure or success in training of military pilots. A follow-up study of abnormal electrocardiograms occurring in this group of fit, young men was initiated at that time. At the end of hostilities Dr. F. A. L. Mathewson continued these studies together with additional cases, and will describe the findings of this follow-up study in a later publication.

INCIDENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES

To continue the earlier electrocardiographic and clinical studies, the Royal Canadian Air Force adopted, eleven years ago, routine electrocardiography as a part of the Aircrew Medical Selection program. During the course of this program we have had an opportunity to study 17,000 electrocardiograms recorded in healthy, fit young men between the ages of eighteen and twenty-four years. Since 1948, definite electrocardiographic abnormalities which cannot be explained by environmental or physiologic factors and which persist on repeat studies have rendered the candidate unfit for pilot training.

The incidence of various electrocardiographic abnormalities found during the course of this study are shown in Table I. In this consecutive series of 17,000 applicants eighty-six candidates were classed as unfit for pilot training (some were accepted for navigator training). From these data it is apparent that significant electrocardiographic abnormalities are uncommon in a large series of healthy, young male subjects. The aircrew candidates with abnormal electrocardiograms were re-examined by a cardiologist. Fifty per cent revealed additional evidence to suggest a cardiovascular disorder. An example of this occurred in a young man who was re-examined because of an abnormal electrocardiogram (Fig. 1), and was found to have an asymptomatic atrial septal defect.

TABLE I

Incidence of Abnormal Electrocardiographic Findings in 17,000 Fit, Healthy Young Men Aged Eighteen to Twenty-Four Years

Abnormality	Total No.	Unfit for Pilot	Abnormality on Electrocardiogram*
T wave variations	489	25	10
Bundle branch block	59	19	9
WPW pattern	33	22	14
Prolonged P-R interval	76	6	3
Miscellaneous	297	14	5
Totals	954	86	41

* This means that the only abnormality found was in the electrocardiogram. In the remainder a cardiac murmur, questionable roentgenogram, elevated blood pressure, questionable history, etc., was found in addition to the electrocardiographic abnormality.

* From the Institute of Aviation Medicine, Royal Canadian Air Force, the Cardiovascular Unit, Department of Medicine, University of Western Ontario, and Victoria Hospital, London, Ontario, Canada.

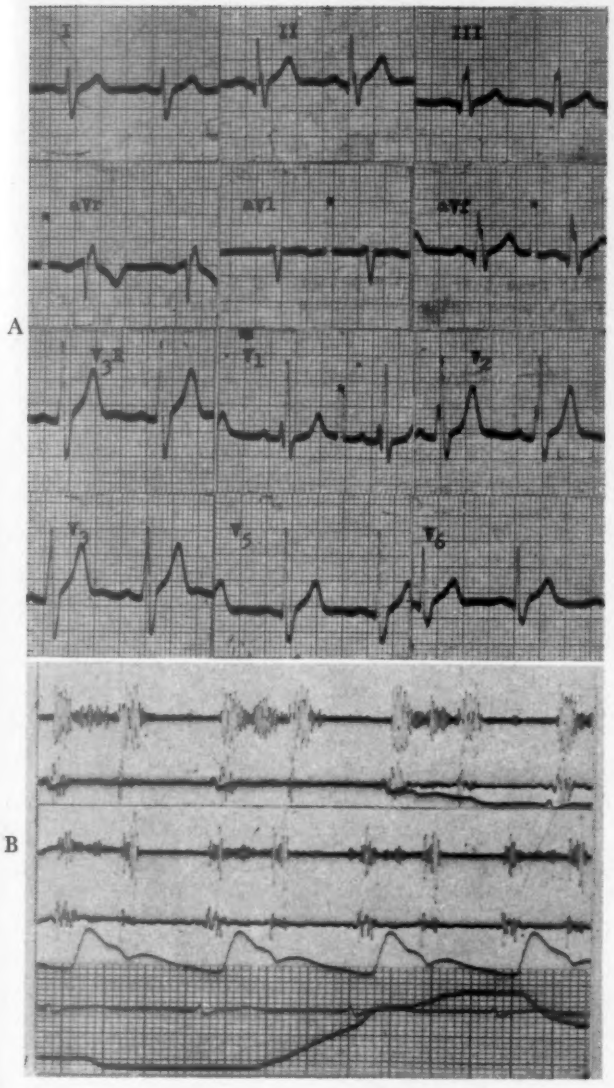


FIG. 1. Tracings obtained from a twenty-three year old subject with asymptomatic atrial septal defect. The electrocardiogram (A) shows right ventricular hypertrophy. The phonocardiographic tracing (B) shows ejection pulmonary systolic murmur and a widely split second heart sound. In (B) the tracings from top to bottom are: pulmonary area, 150–100 c.p.s.; mitral area, low frequency; pulmonary area, 150–150 c.p.s.; mitral area, low frequency; carotid pulse; electrocardiogram; respiration.

There remains, however, a small group (0.2 or 0.3 per cent) in whom the abnormality cannot be explained in the light of our present knowledge (Fig. 2).

Significance of Various Electrocardiographic Changes

It is difficult to assess the significance of an isolated electrocardiographic abnormality in the absence of clinical findings. There are

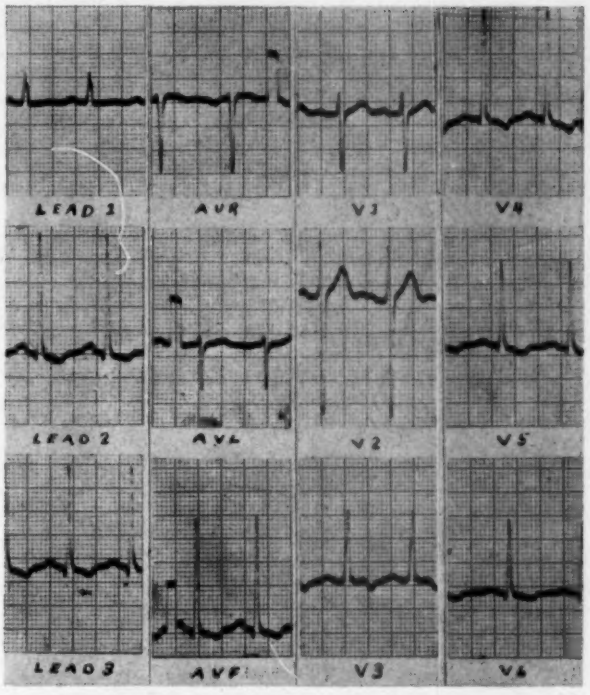


FIG. 2. Tracings obtained from a twenty year old clinically fit applicant. (His twin brother had the same electrocardiographic pattern.) Persistent QRS and T wave abnormality is unexplained and therefore the applicant was considered as unfit for pilot training.

many abnormalities such as prolongation of the P-R interval, right bundle branch block, nonspecific T wave changes, certain ectopic rhythms and the Wolff-Parkinson-White pattern which are considered by some to be of no clinical significance. Some cardiologists believe that any electrocardiographic abnormality occurring in the complete absence of clinical findings should be disregarded. This may be sound medical practice insofar as the patient's welfare is concerned, but there must remain some doubt as to the innocence of the abnormality. Consequently, when some risk is involved, whether it be financial, as in actuarial practice, or responsibility for life and property, as in aviation, such patients must be placed in a somewhat different category.[4]

T Wave Changes: In an earlier series there were ten examples of abnormal T waves in a series of 2,500 routine electrocardiograms.[1–3] Although the follow up is not completed, it is known that some who showed these changes revealed clinical evidence of a cardiac disorder within a few years. One such airman (Fig. 3) died suddenly as he approached his aircraft for take-off one year after the T wave changes were discovered. This man was in apparent good

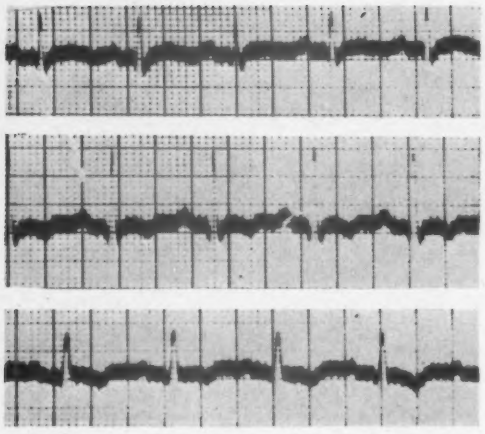


FIG. 3. Tracings obtained from a twenty-seven year old fighter pilot. Leads I, II and III were recorded in 1941, one year prior to sudden fatal episode while approaching aircraft. Note unexplained abnormal T waves.

health and had completed his flying training. He was serving as a Fighter Command Pilot, and had made a number of operational flights. The cause of death was reported as coronary thrombosis. Other examples have occurred in which the electrocardiogram indicated a cardiac disorder not recognized clinically.

There are many examples of non-specific T wave changes which can be explained on the basis of environmental factors, and which we believe should be considered of no clinical significance (Fig. 4). During the recent past, all tracings with questionable T wave findings have been repeated in a fasting state. In a study of 2,000 cases, approximately 3 to 4 per cent of healthy, young males revealed questionable to abnormal T wave changes which were normal in the fasting state[5] (Table II). Furthermore, on further study many examples of significant first degree A-V block have been shown to be normal in the standing position[6] (Fig. 5). On careful clinical examination these men revealed no abnormalities. Since administration of atropine also reduced the P-R interval to normal in this group, it would appear that an autonomic reflex (probably the carotid sinus) was responsible for this change.

TABLE II

T Wave Variations in 2,000 Routine Electrocardiograms

Variation	No.
Total variations	163
Minor variations	82
Gross abnormality	3
Postprandial*	78
Inverted	29
Flat	49

* Fasting tracing normal.

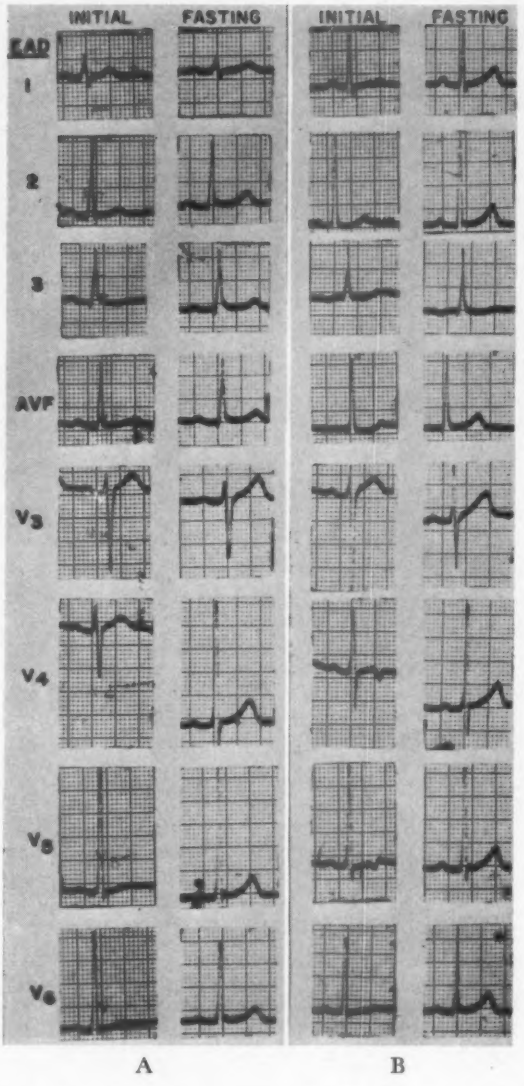


FIG. 4. A, a fit young man aged eighteen years. Note increased amplitude of T waves, especially in leads V_4, V_5 and V_6 after fasting. B, a fit young man aged seventeen years. Note change from negative T waves in leads I, V_4 and V_5 to normal upright T waves after fasting.

Evaluation of Normal Measurements: During the course of this work many observations of the limits of normal for such measurements as wave amplitudes and time intervals in the young age group have been possible. In addition, a number of concepts or criteria used in the electrocardiographic assessment of patients have been studied. Studies in the normal values of the frontal and spatial QRS-T angle, effect of exercise, etc., have also been carried out. Al-

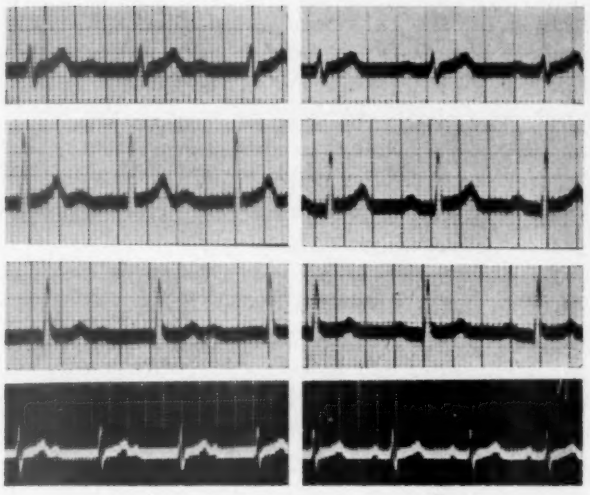


FIG. 5. Postural heart block in a healthy, fit young man. A, recumbent. B, standing.

though these findings are not within the scope of this paper, I would like to refer briefly to an early observation of Ashman and Hidden,[7] and Dressler and Roesler[8] with regard to the T_1 :T_3 ratio. Our findings in this regard indicate that the relation T_1 less than T_3, R_1 greater than R_3, in the absence of the $S_1S_2S_3$ pattern is an extremely rare finding in the normal subject. We believe that this provides a simple and rapid method of indicating an abnormal ventricular gradient or QRS-T angle (Fig. 6).

VALUE OF ROUTINE ELECTROCARDIOGRAPHY

It is difficult to decide how much importance should be attached to an isolated electrocardiographic abnormality. If clinical evidence of some cardiac defect becomes apparent when the repeat studies are performed, the decision is not difficult. It is interesting to note that in many instances, when repeat studies were carried out, additional clinical cardiovascular findings were observed which either had been overlooked or considered to be insignificant at the time of the initial examination. These men, however, would have been permitted to undertake pilot training if routine electrocardiograms had not been taken during the initial selection procedures.

From our experience, and taking into consideration all the factors involved, including the high cost of training aircrew personnel, we believe that routine electrocardiography is of value in the selection of aircrew members, and that subjects having definite abnormalities should not be accepted for aircrew training. (By abnormality is meant a definite electrocardiographic abnormality which persists, and cannot be explained on an environmental, physiologic or other basis not indicative of organic heart disease.)

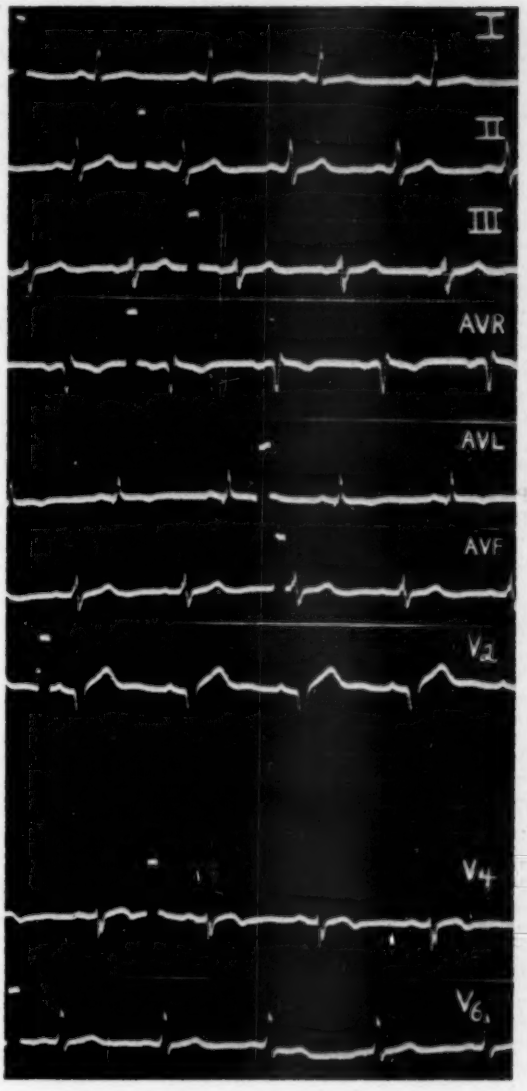


FIG. 6. T_1 less than T_3, R_1 greater than R_3 in a patient with myocardial damage due to coronary artery disease.

Electrocardiographic Standards for Aircrew Acceptance: Considering the question of the suitability of a candidate for aircrew training, it is important that a just and sensible decision be made, both from the point of view of the candidate and of the service. Having carried out our preliminary studies with regard to the use of electrocardiography in the selection of aircrew personnel, and particularly since sufficient data are not yet available from our follow-up studies, we conducted a survey of expert opinions for comparison with our conclusions made follow-

TABLE III
Royal Canadian Air Force Opinion Survey of Thirty Cardiologists

Electrocardiographic Abnormality	Percentage of Consultants Rejecting Applicant
Obvious T wave abnormalities	82
Heart block	
P-R interval greater than 0.24 sec.	67
Incomplete	100
Complete	96
Ectopic rhythms	
Paroxysmal auricular tachycardia	93
Paroxysmal auricular flutter	96
Paroxysmal auricular fibrillation	100
Persistent ectopic auricular rhythm	67
A-V nodal escape	59
A-V nodal tachycardia	93
Frequent ventricular extrasystoles not abolished by exercise	67
Bigeminal ventricular rhythm	74
Short runs of 3 to 4 ventricular extrasystoles	85
Pattern of left ventricular hypertrophy	63
Pattern of right ventricular hypertrophy	63
Right axis deviation and tall or notched P waves	50
Low voltage QRS (all under 5 mm.)	52 (if persists)
QRS greater than 0.12 sec.	74
Right bundle branch block	63
Left bundle branch block	89
WPW syndrome	81

ing the study of the Royal Canadian Air Force experience[9] (Table III). The majority of those consulted agreed with the conclusions of the Royal Canadian Air Force with regard to electrocardiographic standards for acceptance into aircrew training. It is possible that a number of these electrocardiographic abnormalities are associated with congenital or physiologic conditions of no clinical significance, and without risk to life, but because of the small numbers concerned (0.5 per cent) the conclusion has been reached that it is not justifiable to accept for aircrew training applicants who, in the absence of clinical signs and symptoms, have significant electrocardiographic abnormalities which cannot adequately be explained.

The value of routine electrocardiography in selection of pilots might be questioned since it may lead to unjustifiable rejection of the applicant. If, however, it is used sensibly, and in the light of the clinical findings, then it is well worthwhile, not only from the standpoint of selection, but also for future reference. In the last 17,000 applicants eighty-six were rejected as the result of the routine electrocardiogram. However, on further study 50 per cent of these men did present additional clinical findings which might suggest a cardiac abnormality.

In any case in which a questionable electrocardiographic abnormaltiy is found, a careful and thorough clinical examination, including a number of further electrocardiographic studies, should be carried out; otherwise the rejection rate will jump unjustifiably from 0.2 or 0.3 per cent to 5 per cent or more (Table I). Although the electrocardiogram has led to many mistakes in its use in the diagnosis of heart disease, a normal electrocardiogram is reassuring in the assessment of our subjects. If the electrocardiogram has any place in selecting subjects in the young (military) age group who may be candidates for future myocardial disease, study and follow up on those who reveal minor abnormalities, and particularly the effect of stress on the electrocardiogram, are required for some time to come. The problem of electrocardiographic evaluation as an indication of premature coronary narrowing remains complex, and is still a challenge to the inquiring and critical cardiologist concerned with aviation.

SUMMARY

In this study the electrocardiograms of 17,000 fit Royal Canadian Air Force aircrew applicants between the ages of eighteen and twenty-four have been reviewed. In 954 instances abnormalities of varying degrees were observed and repeat electrocardiographic studies, including further investigation, were carried out by a cardiologist in all but a few instances.

There were eight-six applicants classed as unfit for pilot training on the basis of an abnormal electrocardiographic finding which could not be explained or accounted for on a physiologic or environmental basis. A few were found to have organic heart disease. A larger number (total of forty-five including proved heart disease) were found to have questionable findings either in the history or on clinical examination (cardiac murmurs, elevated blood pressure, questionable roentgenographic findings, history of tachycardia, syncope, trauma to the chest, infectious diseases, etc.) that may or may not have had some bearing on the electrocardiographic findings. These eighty-six men, how-

ever, were not accepted for pilot training on the basis of the abnormal electrocardiogram.

References

1. Hall, G. E., Stewart, C. B. and Manning, G. W. The electrocardiographic records of 2000 Royal Canadian Air Force aircrew. *Canad. M. A. J.*, 46: 226, 1940.
2. Stewart, C. B. and Manning, G. W. A detailed analysis of the electrocardiograms of 500 Royal Canadian Air Force aircrew. *Am. Heart J.*, 27: 502, 1944.
3. Manning, G. W. Abnormal electrocardiogram found in Royal Canadian Air Force aircrew. Associate Committee on Aviation Medical Research, National Research Council, Canada. Report No. C3179, July 1942.
4. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew. *Circulation*, 10: 401, 1954.
5. Sears, G. A. and Manning, G. W. Routine electrocardiography: post prandial T wave changes. *Am. Heart J.*, 56: 591, 1958.
6. Manning, G. W. and Stewart, C. B. Alteration in P-R interval associated with change in posture. *Am. Heart J.*, 30: 109, 1945.
7. Ashman, R. and Hidden, E. H. Rightward deviation of the axis of the T wave as an index of myocardial disease. *Ann. Int. Med.*, 12: 1682, 1939.
8. Dressler, W. and Roesler, H. The diagnostic values of the pattern T-1 lower than T-3. *Am. Heart J.*, 36: 1948.
9. Manning, G. W. and Fitzgibbon, G. M. Electrocardiography in the selection of aircrew members. *J. Aviation Med.*, 27: 221, 1956.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

I. Incidence of Abnormalities*

CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THIS IS the first of a series of reports on the study of the electrocardiogram in 67,375 asymptomatic, healthy adult men. Previous studies concerned with the incidence of various electrocardiographic abnormalities in smaller groups of apparently healthy male adults, in large groups of hospitalized patients and in persons having specific disease processes have been reported. Ferguson and O'Connell[1] studied the electrocardiograms of 1,812 midshipmen in 1924 who, except for three, were considered free of heart disease. Standard leads I, II and III were recorded. Of these 1,812 electrocardiograms, 944 were considered to be completely normal and the remainder showed various electrocardiographic changes, many of which are known today to be of little significance.

In 1941, Wood, Wolferth and Miller[2] reported their experience in comparing the electrocardiographic findings with the clinical evaluation in groups of unselected students, in college students with suspected heart disease and in unselected corporation executives. In some, standard leads I, II and III were used alone, and in others, a full twelve-lead electrocardiogram was recorded. Their conclusions were: (1) In persons under thirty years of age, electrocardiographic study does not demonstrate cardiac abnormalities of importance from the military standpoint, which are not discernible on physical examination. (2) In persons over thirty years of age, and especially in those over forty, electrocardiographic study may occasionally demonstrate degenerative heart disease before symptoms occur.

Graybiel et al.[3] reported the electrocardiographic findings in 1,000 subjects twenty to thirty years of age, who were involved in naval aviation. All had been selected for flight training after meeting rigid physical qualifications. A number of interesting tracings were observed, including twenty-three instances of wandering pacemaker in and about the S-A node, one case of S-A block with A-V nodal escape, one case of A-V nodal rhythm (P-R interval 0.09 second, with P waves inverted in leads II and III), two cases of Wolf-Parkinson-White (WPW) syndrome, fifteen cases of premature beats (eight ventricular and seven atrial in origin), sixteen cases of prolongation of the P-R interval beyond 0.20 second, one case of complete left bundle branch block and seven additional cases in which the QRS duration was 0.12 second. These fifty cases represented 5 per cent of the total. It should be noted that only leads I, II, III, IVF and IVR were recorded. The authors concluded that electrocardiography is of particular value in the medical evaluation of pilots, particularly if a baseline tracing has been made at an early age, and follow-up tracings are obtained.[4]

In 1954, Manning[5] reported on the electrocardiographic findings in 5,000 healthy adult male applicants for aircraft training in the Royal Canadian Air Force, ranging in age from eighteen to twenty-four years. Significant abnormalities were detected in 151 subjects, or 3 per cent of the total survey. Following further electrocardiographic and clinical studies, 5.4 per 1,000 persons who had been previously passed for pilot training were considered unsuitable. The authors conclude that a routine electrocardiogram on all candi-

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

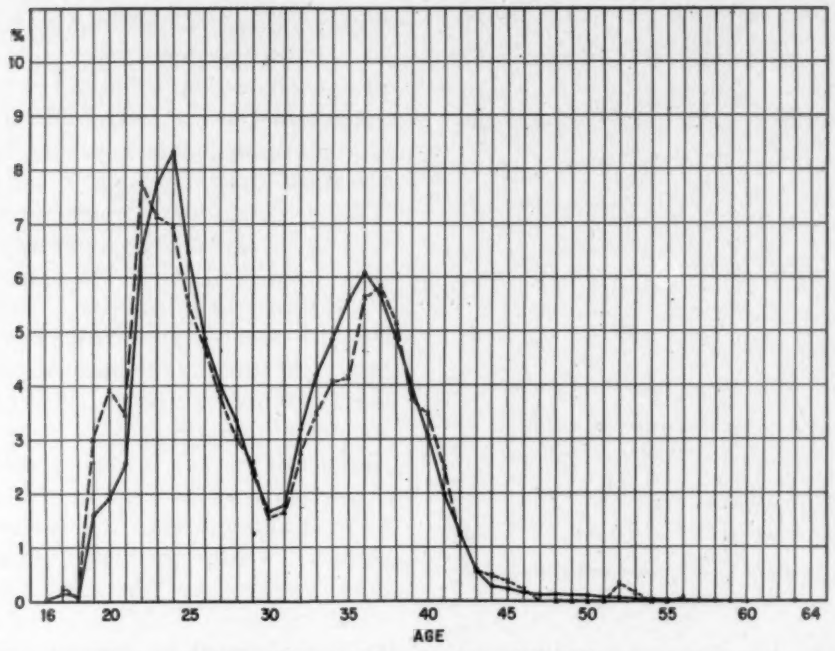


FIG. 1. The percentage of the total population (67,375) surveyed in each age group is depicted by the solid line. The percentage of the total abnormalities is depicted by the broken line. Note that the two curves are quite similar, indicating that the incidence of the total abnormalities is about the same for all age groups.

dates for pilot training is exceedingly worthwhile.

The incidence of electrocardiographic abnormalities in various age groups under varying circumstances has been reported by Brody, Golden and Tobin,[6] Langley[7] and Wolfram.[8]

MATERIAL AND METHODS

In April 1957 a central U. S. Air Force Electrocardiographic Repository was established. It was designated to keep electrocardiograms on all selectees for flight training, a baseline tracing on all rated Air Force officers under the age of forty years; a yearly tracing on all rated officers aged forty and above, and tracings on all rated officers who had electrocardiograms taken during hospitalization, episodes of cardiac arrhythmias, various physiologic training programs, etc. The electrocardiograms were to consist of at least the three bipolar limb leads, three augmented unipolar limb leads and six chest leads V_1 through V_6. Each lead was to be clearly marked, 5 to 6 inches in length and to show one or more standardization marks. These leads were arranged in sequence and forwarded to the USAF Electrocardiographic Repository attached to a standard clinical record giving name, rank, serial number, age, weight, height, race and blood pressure, and designating if the subject was taking any type of medication.

The electrocardiograms reported here are concerned only with those subjects who were asymptomatic and actively engaged in military duties, or who were applying for flying training. They compose a select group of adult men who can be considered to represent each age group in a state as nearly free of disease as possible.

RESULTS

Figure 1 shows the age distribution for the total survey on which is superimposed the age distribution of those with electrocardiographic abnormalities. They are nearly identical. Worth noting is the fact that very close to 90 per cent of these subjects were between the ages of twenty and forty, less than 10 per cent were over the age of forty and less than 2 per cent under the age of twenty. The mean age was 30.7 years, but this is not a significant figure when the configuration of the distribution curve is noted. A total of 2,527 electrocardiographic abnormalities was found in the 67,375 electrocardiograms. These were found in 2,499 subjects, which represents 3.7 per cent of the entire survey, or 37.6 per 1,000 subjects.

The distribution of abnormalities makes it apparent that certain electrocardiographic abnormalities are more common in youth and may be unrelated to heart disease. This group commonly includes atrial rhythm, nodal rhythm, wandering pacemaker, A-V dissociation and sinus arrest. A curve of the per cent of total

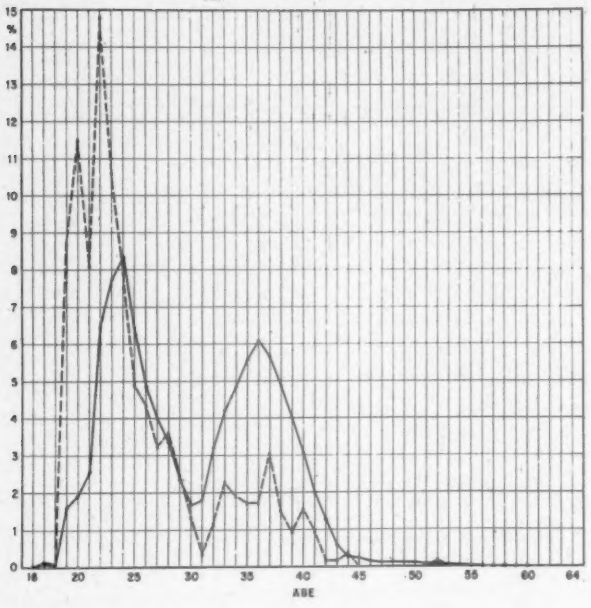


FIG. 2. The solid line represents the percentage of the population in each age group. The broken line represents the percentage of 527 abnormalities in each age group representing atrial rhythm, wandering pacemaker, A-V dissociation, nodal rhythm and sinus arrest. The high peak for abnormalities in the younger age groups demonstrates the increased incidence of these abnormalities in younger subjects.

abnormalities for each age group superimposed on the survey population distribution demonstrates the marked influence of youth on the frequency of these abnormalities (Fig. 2). Other abnormalities, with a higher incidence in the older age group, include T wave changes, ventricular premature contractions, right bundle branch block, tracings suggestive of old myocardial infarction, left bundle branch block and atrial flutter or fibrillation. A curve of the incidence of these abnormalities compared to the age distribution of the population surveyed shows the influence of age on the frequency of these abnormalities (Fig. 3). This is particularly significant since it is likely that these particular abnormalities detected in the age group past forty commonly lead to suspension from flying duties. Thus, the true incidence of these abnormalities past the age of forty is probably much greater. The T wave changes appeared to be increased in incidence in the younger subjects and again after the age of forty years.

Still another group of findings appears to occur with approximately the same frequency, regardless of age. These include first degree A-V block, supraventricular premature contractions, the WPW syndrome and ventricular parasystole.

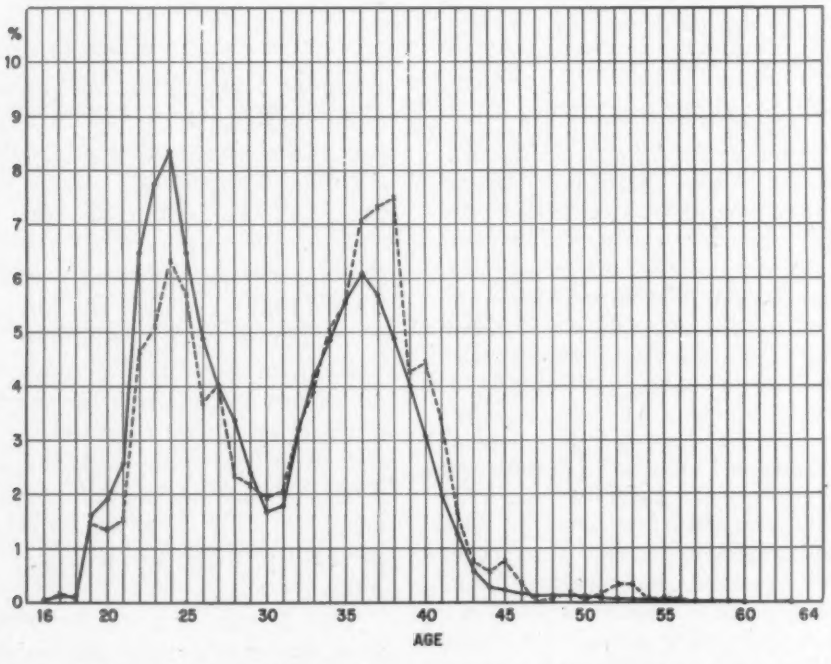


FIG. 3. The solid line represents the percentage of the population in each age group. The broken line represents the percentage in each group of 1,190 abnormalities that include T wave changes, ventricular premature contractions, right bundle branch block, possible myocardial infarction, left bundle branch block, and atrial flutter or fibrillation. The curve of abnormalities demonstrates an increased incidence of these abnormalities in the older age groups.

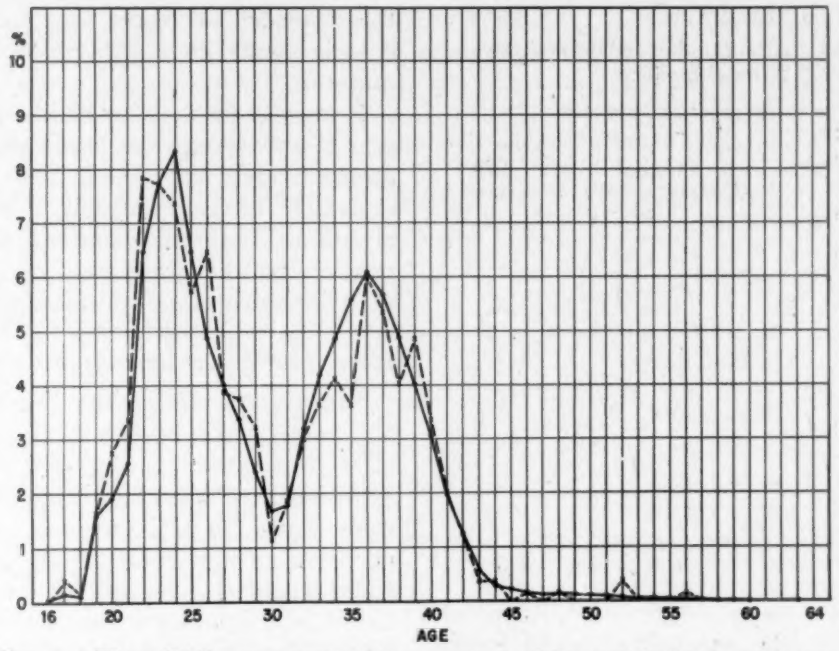


FIG. 4. The solid line represents the percentage of the population in each age group. The broken line represents the percentage in each group of 803 abnormalities that include first degree A-V block, supraventricular premature contractions, WPW syndrome and ventricular parasystole. The similarity of the two curves demonstrates that the incidence of these abnormalities is not particularly influenced by the age of the subjects in this survey.

The frequency of these findings in the various age groups as compared to the distribution by age of the population studied is seen in Figure 4.

Table I lists each abnormality found, the total number having each abnormality, the per cent of each abnormality of the total abnormalities and the rate per 1,000 subjects. To determine if a specific abnormality was more frequent in one age group, the age distribution for each abnormality was compared to the age distribution for the entire survey. Table II shows the age-specific abnormality per 1,000 subjects for each age group, and summarizes the data which are to be more thoroughly discussed under the individual electrocardiographic abnormalities.

SUPRAVENTRICULAR ARRHYTHMIAS

Sinus Arrest with Supraventricular Escape Beats: Five subjects were seen with this mechanism alone, four with nodal escape beats and one with atrial escape.

Atrioventricular Dissociation: Thirty-three instances were found in which A-V dissociation was apparent. Although the total number was small, it was apparent that this arrhythmia was found predominantly in the younger subjects since twenty-seven of the thirty-three were under the age of twenty-five years.

Atrial Rhythm: Atrial rhythm, in which a focus in the atria becomes the cardiac pacemaker, was found in 328 subjects representing 13 per cent of the total abnormalities. The incidence was 4.9 per 1,000 subjects. A statistically significant concentration of these was found in the younger subjects (Table II).

Atrial Flutter and Fibrillation: Only five records showed this gross abnormality, all in asymptomatic subjects on full military duty.

Nodal Rhythms: Only nine subjects were classified as demonstrating a nodal rhythm. The difference in incidence when nodal arrhythmias are compared to atrial arrhythmias is striking.

Wandering Pacemaker: There were 152 subjects who showed some wandering of the cardiac pacemaker. Only two of these subjects appeared to have wandering pacemaker to the A-V node. A significantly greater number were in the younger age groups.

VENTRICULAR ARRHYTHMIAS

Ventricular arrhythmias were rare in this study when ventricular premature beats were excluded.

Idioventricular Rhythm: Three pilots on full military duty, whose ages were twenty-three, thirty-two and thirty-seven, were found to have

TABLE I

Summary of Electrocardiographic Abnormalities in 67,375 Normal Subjects

Abnormality	No.	Per Cent of Total Abnormalities	Abnormalities per 1,000 Subjects
Non-specific T wave and S-T segment changes	581	23.0	8.6
Ventricular ectopic beats*	419	16.6	6.2
First degree A-V block	350	13.8	5.2
Supraventricular premature contractions	329	13.0	4.9
Atrial rhythm	328	13.0	4.9
Wandering pacemaker	152	6.0	2.3
Right bundle branch block	106	4.2	1.6
WPW syndrome	106	4.2	1.6
Possible myocardial infarction	66	2.6	1.0
A-V dissociation	33	1.3	0.5
Ventricular parasystole	18	0.7	0.3
Left bundle branch block	13	0.5	0.2
Nodal rhythm	9	0.4	
Sinus arrest with escape	5	0.2	
Atrial flutter and fibrillation	5	0.2	
Idioventricular rhythm	3	0.1	
Second degree A-V block	1	0.0	
Complete A-V block	1	0.0	
Right ventricular hypertrophy	1	0.0	
Ventricular tachycardia	1	0.0	
Total abnormalities	2,527	...	37.6

* Not including parasystole.

an intermittent idioventricular rhythm. In all three instances the baseline tracing showed A-V dissociation with the ventricles being stimulated by a focus apparently originating in the right ventricle.

Ventricular Tachycardia: One subject, aged thirty-five years, was found to have frequent premature ventricular contractions with intermittent ventricular tachycardia as defined by the presence of three successive ventricular ectopic beats at a rate faster than 100 per minute.

Ventricular Parasystole: Eighteen electrocardiograms were consistent with parasystole originating from a ventricular focus.[9] These demonstrated typical ventricular fusion beats or premature ventricular contractions with varying relation to the preceding normal beats and not apparently of multifocal origin.

PREMATURE CONTRACTIONS AND EXTRASYSTOLES

Supraventricular ectopic beats were noted in 329 records comprising 12.9 per cent of the total abnormalities (4.9 per 1,000 subjects). Ventricular ectopic beats (including parasystole) were noted in 437 records representing 17 per cent of the total abnormalities (6.5 per 1,000 subjects). No significant difference was found in the incidence of the supraventricular ectopic beats among the various age groups, but a definite increase in the older age groups was apparent in those ectopic beats originating from a ventricular focus.

INTRAVENTRICULAR CONDUCTION DEFECTS

Only those records showing the WPW syndrome, complete right bundle branch block and complete left bundle branch block are included here. No record was included with the WPW syndrome in which the QRS complex had a normal configuration. Only records showing complete right bundle branch block were included. Records showing a QRS duration of less than 0.12 second, in which the terminal forces were directed to the right, were not included. These three specific abnormalities totaled 225 records, comprising 9 per cent of the total abnormalities, or a rate of 3.3 per 1,000 subjects. WPW syndrome was observed in 106 records, right bundle branch block in 106 and left bundle branch block in thirteen. Of interest is the fact that the WPW syndrome was as frequent as right bundle branch block. There was no significant difference in the frequency of the WPW syndrome in the various age groups, but right bundle branch block tended to occur more frequently at forty-five years of age or older (Table II).

ATRIOVENTRICULAR BLOCK

First Degree A-V Block: A total of 350 subjects, comprising 13.8 per cent of the total abnormalities, had electrocardiograms which showed a

TABLE II

Incidence Rate per Thousand in Different Age Groups for Certain Electrocardiographic Abnormalities

Age (yr.)	Non-specific T and S-T Changes	Ventricular Ectopic Beats*	Supraventricular Ectopic Beats	First Degree A-V Block	Atrial Rhythm	Wandering Pacemaker	Right Bundle Branch Block	WPW Syndrome	Possible Myocardial Infarction
16–20	11.1	4.7	4.0	5.5	21.9	7.9	...	3.2	...
20–24	5.2	5.4	5.3	6.0	9.0	5.0	1.2	1.8	0.3
25–29	8.9	4.4	5.7	5.1	4.6	1.9	1.1	1.6	0.6
30–34	7.2	7.7	4.0	4.6	2.0	1.2	2.1	1.8	1.3
35–39	11.4	6.4	4.6	4.7	1.7	0.7	1.8	1.3	1.5
40–44	12.0	10.7	4.0	6.2	3.5	...	2.7	1.0	1.5
45 +	19.0	16.1	4.4	3.0	1.4	...	4.4	2.9	4.4
Total group	8.6	6.2	4.9	5.2	4.9	2.3	1.6	1.6	1.0

* Excluding parasystole.

delay in conduction between the atria and ventricles, an incidence of 5.2 per 1,000 subjects. No significant difference was seen in the incidence of first degree A-V block in the various age groups. First degree A-V block was defined as a P-R interval of 0.21 second or greater when the heart rate was below 100 per minute, or a P-R interval of 0.20 second or over when the heart rate was over 100 beats per minute. Of interest is that only forty-five of these 350 subjects had a P-R interval of 0.25 second or greater, representing less than 1 per 1,000 subjects.

Second Degree A-V Block: One subject showed this finding associated with a typical Wenkeback phenomenon.

Complete A-V Block: One subject had complete A-V block. He was a twenty-six year old pilot on full flying duty.

S-T SEGMENT AND T WAVE CHANGES

A total of 581 subjects, representing 23 per cent of the total abnormalities, demonstrated S-T segment or T wave changes. The incidence rate was 8.6 per 1,000 subjects. Table II shows that the rate per 1,000 subjects increased significantly in the older age groups. Minimal decrease in T wave amplitude alone was not included in this group.

Of particular interest is the fact that twenty-one of these 581 individuals were Negroes. Whereas the incidence of T wave changes was 8.6 per 1,000 subjects in the entire study, the incidence rate of T wave changes for the Negro was 51 per 1,000 subjects.

ELECTROCARDIOGRAMS SUGGESTIVE OF MYOCARDIAL INFARCTION

Sixty-six electrocardiograms, representing 2.6 per cent of the total abnormalities, were considered to be suggestive of myocardial infarction. This produced an incidence rate of 1 per 1,000 subjects. The criteria required for electrocardiographic diagnosis included *all* of the following:

Inferior (Diaphragmatic) Wall Infarction: (1) Q_3 of at least 0.04 second duration and followed by an R wave; (2) Q_{aVF} of at least 0.02 second duration; (3) Q_2 must be present; (4) intraventricular conduction must be normal; (5) the amplitude of the QRS complex in lead III must be at least 5 mm. (0.5 mv.), unless Q_3 is greater than 2.5 mm. (0.25 mv.); (6) if the rhythm is sinus, P_3 must be upright, with an isoelectric interval between the P and Q waves.

Anterior Wall Infarction: (1) R waves must be absent in leads V_1, V_2 and V_3, or there must be localized loss of R wave amplitude in leads V_2, V_3 or V_4; (2) the P wave must be upright in lead V_2.

Records were considered borderline for inferior wall infarction if all the critera were met except that P_3 was diphasic or inverted. Records were considered borderline for anterior wall infarction if all the criteria were met except that tiny R waves were present in lead V_3.

These sixty-six subjects had a tendency to be in the older age groups (Table II).

MISCELLANEOUS ABNORMALITIES

Ventricular Hypertrophy: Only one record was considered to be compatible with right ventric-

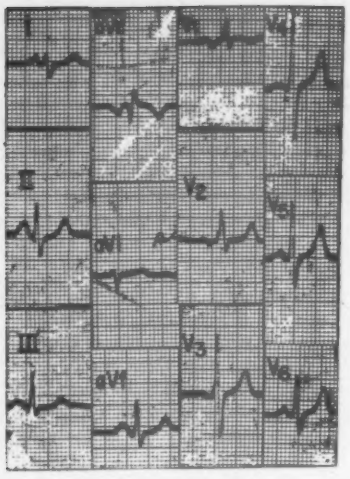


FIG. 5. This routine electrocardiogram was thought to represent right ventricular hypertrophy and atrial enlargement. Clinical examination confirmed the presence of mitral stenosis.

ular hypertrophy. This was in a thirty-six year old pilot on full flying duty. There were also associated marked P wave changes suggesting atrial hypertrophy (Fig. 5). This officer was found to have classic findings of mitral stenosis with pulmonary hypertension, right ventricular and left atrial enlargement. No records were found which could be definitely classified as showing left ventricular hypertrophy in subjects who were not known to have heart disease or some degree of arterial hypertension. Borderline cases which might be considered as evidence of hypertrophy were included in the electrocardiograms classified as showing non-specific T wave changes.

Non-specific Intraventricular Conduction Defects: Those subjects whose tracings showed only axis deviation to the right or left, non-specific increases in QRS duration, QRS notching, etc., have not been included in this statistical survey.

OBSERVATIONS ON THE ELECTROCARDIOGRAM IN NEGROES

There were 410 Negroes in this survey, representing 0.61 per cent of the total population. Thirty-nine, or 9.5 per cent, had electrocardiographic abnormalities. This is a significantly higher figure when compared to the abnormal rate for the white population, which was 3.1 per cent. The difference was due primarily to the increased incidence of first degree A-V block and T wave changes in the Negro population. Table III lists the electrocardiographic abnormalities found in the 410 Negroes included in this survey.

TABLE III
Incidence of Electrocardiographic Abnormalities Found in 410 Negroes in the Survey

Abnormality	No.
Atrial rhythm	1
Supraventricular premature beats	2
Ventricular premature beats	3
WPW syndrome	1
Right bundle branch block	1
First degree A-V block	7
T wave changes	21
Possible infarction	1
Parasystole	1
Wandering pacemaker	1
Total	39

COMMENTS

The electrocardiographic abnormalities listed in Table I accounted for 3.7 per cent of the population surveyed, or 37.6 per 1,000 subjects. Those electrocardiographic abnormalities more commonly associated with clinical heart disease accounted for a smaller, but still significant number. It is also important to realize that some changes of cardiac rhythm which are not usually considered clinically important are of extreme importance when combined with the acute physical stresses sometimes encountered during flight.

It is hoped that the baseline tracings recorded on each subject, even when normal, will be valuable for the detection of future electrocardiographic changes produced by asymptomatic coronary artery disease.

To further define the importance of the various electrocardiographic abnormalities observed in this survey, the subjects will need a comprehensive cardiovascular evaluation and long term follow up. Subsequent reports will deal with a clinical evaluation of the subjects whose baseline electrocardiograms were abnormal.

SUMMARY

The electrocardiograms obtained from 67,375 asymptomatic healthy adult men have been studied to determine the incidence of electrocardiographic abnormalities.

There were 2,527 electrocardiographic ab-

normalities in 2,499 subjects, representing 3.7 per cent of the total population surveyed.

The age distribution curve for the total abnormalities was almost identical to the age distribution curve for the sampled population.

With increasing age, there was a significant increase in incidence of non-specific T wave changes, ventricular ectopic beats, right bundle branch block, and possible myocardial infarction, and a significant decrease in incidence of simple atrial rhythm and wandering pacemaker.

There was no significant difference in incidence among the various age groups for those records showing supraventricular ectopic beats, first degree A-V block or the WPW syndrome.

The subjects with A-V dissociation were concentrated in the younger age groups, with twenty-seven of the thirty-three subjects with this abnormality being less than twenty-five years of age.

The electrocardiograms obtained from 410 Negro officers in the Air Force had a 9 per cent abnormality rate compared to a 3.1 per cent abnormality rate for the non-Negro population. The source of this increased abnormality rate was found in the increased incidence of T wave changes and first degree A-V block.

Acknowldgment

We wish to thank the Department of Biometrics, School of Aviation Medicine, for its cooperation in tabulating the data in this study; in particular the suggestions and assistance of Miss Margaret Allen were indispensible to the success of the survey. We also wish to express our gratitude to Mrs. Louise Kelly whose continued hard work as supervisor of the USAF Electrocardiographic Repository provided for the efficient and rapid processing of the large number of records involved in this study. Finally, we wish to thank all the medical personnel in the Air Force without whose cooperation this project would have been impossible.

References

1. Ferguson, D. O. and O'Connell, J. T. Cardiovascular observations: electrocardiograms on men without heart symptoms. *U. S. Navy M. Bull.*, 24: 860, 1926.
2. Wood, F. C., Wolferth, C. C. and Miller, T. G. Electrocardiography in military medicine. *War Med.*, 1: 696, 1941.
3. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
4. Packard, J. M., Graettinger, J. S. and Graybiel, A. Analysis of the electrocardiograms obtained from 1000 young healthy aviators. Ten year follow-up. *Circulation*, 10: 384, 1954.
5. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew *Circulation*, 10: 384, 1954.
6. Brody, J. I., Golden, L. H. and Tobin, J. L. Right bundle branch block in young hospitalized males. *New England J. Med.*, 256: 250, 1957.
7. Langley, R. W., Reed, J. C. and Utz, D. C. Bundle branch block, a review of 100 cases. *Am. Heart J.*, 33: 730, 1947.
8. Wolfram, J. Bundle branch block without significant heart disease. *Am. Heart J.*, 41: 656, 1951.
9. Pick, A. Parasystole. *Circulation*, 8: 243, 1953

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

II. Supraventricular Arrhythmias*

CAPT. ROBERT J. FOSMOE, MC, USAF, CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THIS IS the second of a series of reports of electrocardiographic findings found in an asymptomatic, healthy flying population of 67,375 male subjects. The present report is concerned with the 861 instances of supraventricular arrhythmias noted. These include sinus arrest, wandering pacemaker, atrial rhythm, atrial tachycardia, atrial fibrillation, nodal rhythms, A-V dissociation and supraventricular premature contractions.

No large survey of subjects with disturbances of supraventricular rhythm in an asymptomatic population has been published. Graybiel et al.,[1] in an analysis of electrocardiograms obtained from 1,000 naval aviators, found only one case of A-V nodal rhythm and one instance of S-A block with A-V nodal escape. In 1954, Manning[2] reported on 151 subjects with abnormal electrocardiographic findings among 5,000 healthy adult men. Only one of these was found to have a supraventricular arrhythmia, this being a case of paroxysmal atrial tachycardia.

MATERIAL AND METHODS

Sixty-five of the 861 asymptomatic subjects with supraventricular arrhythmias have been seen in consultation at the School of Aviation Medicine and an intensive cardiovascular evaluation has been carried out in each case. The evaluation included a thorough physical examination, an additional twelve-lead electrocardiogram, a complete blood count, urinalysis, fasting blood sugar, serum cholesterol and phospholipids. Posteroanterior and left lateral roentgenograms were recorded in all and additional roentgenographic studies were carried out when indicated. Special electrocardiographic procedures, utilizing a four-channel instrument, were accomplished in all cases. These included continuous tracings during rhythmic deep breathing, postural changes with the subject lying, sitting, and standing, breath-holding, hyperventilation followed by breath-holding, carotid sinus massage, and following rapid intravenous injection of atropine sulfate (1.2 mg.). A double Master exercise test was carried out in the majority and quantitative vectorcardiographic analysis was also accomplished in most subjects.

An additional forty-three subjects demonstrating atrial rhythm were evaluated under standardized conditions at their home base. The evaluation included a thorough physical evaluation, roentgenogram of the chest, and blood sugar and serum cholesterol determinations. The electrocardiogram was repeated with the subject lying down and in the fasting state. A double Master exercise test was performed in all cases. Special electrocardiographic

TABLE I

Supraventricular Arrhythmias in 67,375 Electrocardiograms

Sinus arrest with supraventricular escape beats		5
A-V dissociation		33
Passive	32	
Active	1	
Atrial rhythm		328
Passive	311	
Active	17	
Atrial fibrillation		5
Nodal rhythm		9
Passive	6	
Active	3	
Wandering pacemaker		152
In atria only	150	
In A-V node	2	
Atrial and nodal premature contractions		329
Total		851

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

procedures included the recording of a twelve-lead electrocardiogram during a complete respiratory cycle (deep inspiration, breath-holding for fifteen seconds and expiration) and during orthostasis (immediately on standing and after standing three minutes). Direct communication with the physician who examined these subjects was carried out in most instances.

The remainder of the subjects with supraventricular arrhythmias have not been studied further because of limitations in facilities.

Results

The incidence of the various abnormalities is given in Table 1. The most frequent arrhythmias were atrial rhythm (including upper nodal rhythm and coronary sinus rhythm) and supraventricular premature beats.

ATRIAL RHYTHM

There were 328 instances of simple atrial rhythm in which a focus in the atria became the cardiac pacemaker while a routine twelve-lead electrocardiogram was being obtained. The change in cardiac pacemaker is usually manifested by a marked change in the P vector with slowing of the cardiac rate. The P-R interval is usually normal, commonly 0.10 second or greater (Fig. 1). Instances of atrial rhythm represent 13 per cent of all abnormalities found in the electrocardiographic survey. The incidence was 4.7 per 1,000 subjects. A statistically significant concentration of these

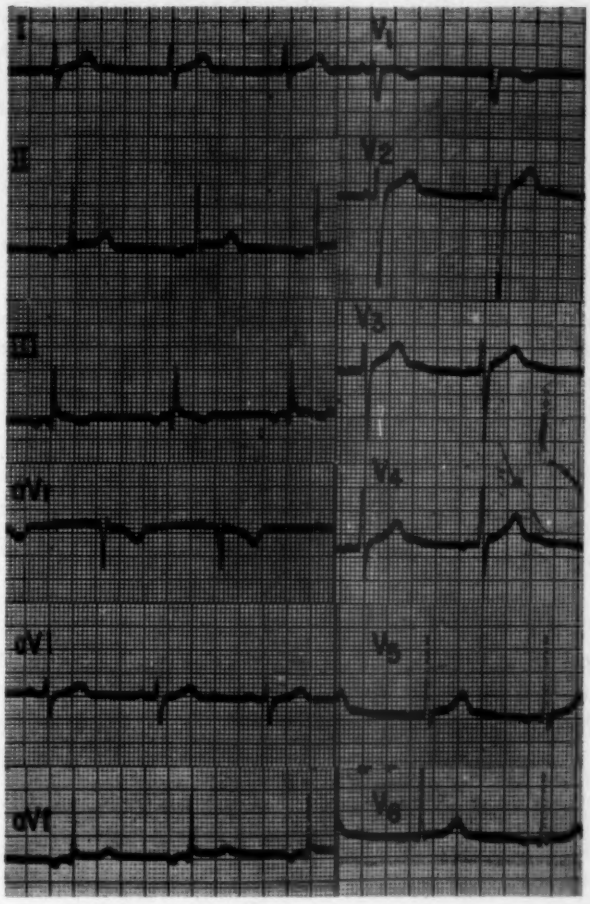


Fig. 1. Uncomplicated atrial rhythm with a normal P-R interval of 0.18 second and retrograde atrial excitation.

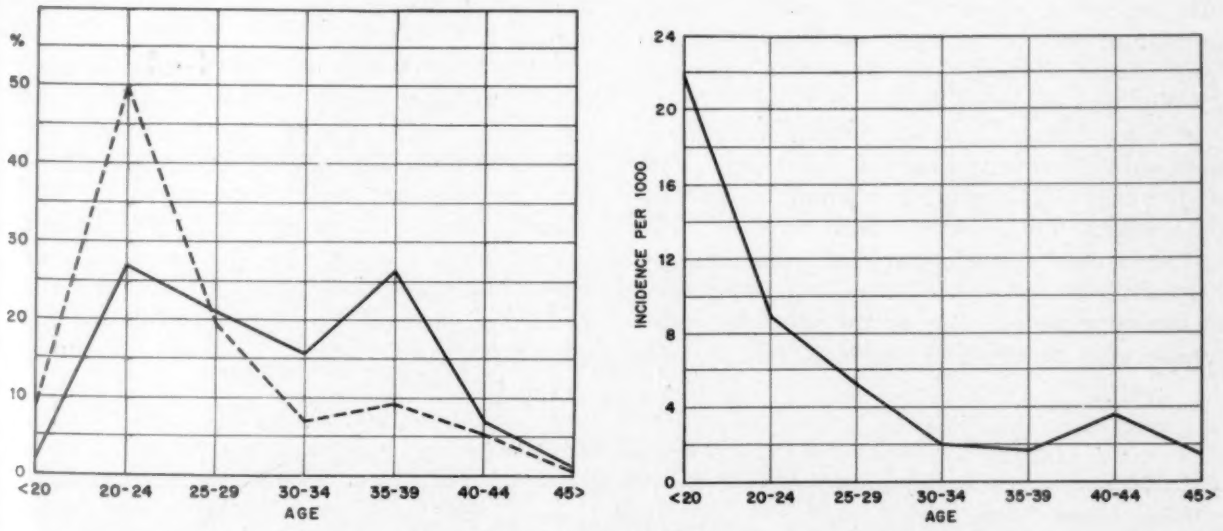


Fig. 2. Incidence of atrial rhythm. *Left*, the solid line depicts the per cent of the total population surveyed in each age group. The broken line depicts the per cent of atrial rhythms found in each group. Comparison of the two curves clearly demonstrates the increased incidence of the atrial rhythm in the younger age group. *Right*, the curve of the incidence per thousand of atrial rhythm for different age groups demonstrates the marked increased incidence of this finding in the younger age groups.

TABLE II
Distribution of P Wave Axis in Frontal Plane During Atrial Rhythm

During Atrial Rhythm

P wave axis (degrees)	−15	−30	−45	−60	−75	−90	−105	−120	−150	+150	Tota
No. of subjects	3	93	45	23	25	60	4	6	2	1	262
Per cent	1.1	94.0					4.9				100

During Normal Sinus Rhythm

P wave axis (degrees)	−15	0	+15	+30	+45	+60	+75	+90	Total
No. of subjects	1	5	3	26	51	30	25	3	144
Per cent	6.3			91.6				2.1	100

was found in the younger individuals. Fifty-eight per cent of the individuals were twenty-four years of age or younger, while only 29 per cent of the entire population surveyed were in this age group. The rate per 1,000 subjects was 21.9 below the age of twenty, and 9 per 1,000 between the ages of twenty and twenty-four. The rate was only 3 per 1,000 at age twenty-five or older (Fig. 2).

When atrial rhythm began after a longer interval following the preceding sinus beat and continued at a slower rate than the basic sinus rhythm, it was classified as passive atrial rhythm. This occurred in 311 instances. In seventeen subjects, atrial rhythm began with an atrial premature beat or the rate was faster than the basic sinus rhythm. In these subjects, the rhythm was classified as active atrial rhythm.

P Wave Changes: Atrial rhythm was associated with a marked change in the P wave. In 94 per cent of 262 subjects in whom it could be determined, the P vector was between −45 and −90 degrees during atrial rhythm. It was between +30 and +75 degrees in 91.6 per cent of the same persons during the time the pacemaker was in the S-A node (Table II). In ninety-eight electrocardiograms the change in P axis resulting from the change in pacemaker could be calculated. In 84.7 per cent of these, the direction of the P vector changed 75 to 165 degrees when the pacemaker shifted from the S-A node to a site lower in the atrium (Table III). In nearly all cases of atrial rhythm, the P axis was equal to, or greater than, −30 degrees, giving biphasic to inverted P waves in lead II and inverted P waves in leads III and aVF. In three subjects, the P axis was only −15 degrees, but the change in P wave contour was so marked compared to the P wave during periods of sinus rhythm, that it was clear that a change in the location of pacemaker to an atrial focus had occurred.

Changes in P-R Interval: In the cases of intermittent atrial rhythm, the P-R interval showed remarkably little change as the pacemaker shifted from the S-A node to the atrium (Table IV). In 98.9 per cent of the cases, the P-R interval was 0.12 second or greater during normal sinus rhythm. In 86.7 per cent of the same subjects demonstrating P wave inversion and atrial rhythm, the P-R interval was 0.12 second or greater. In 172 records the change

TABLE III
Change in P Wave Axis During Conversion from Normal Sinus Rhythm to Atrial Rhythm

Change (degrees)	30	45	60	75	90	105	120	135	150	165	180	195	Total
No. of Subjects	2	2	8	17	9	13	20	10	11	3	1	2	98
Per Cent	12.2			84.7							3.1		100

TABLE IV
Atrial Rhythm: Distribution of P-R Intervals

During Atrial Rhythm

P-R interval (sec.)	0.10	0.11	0.12	0.13	0.14	0.15	0.16	0.17	0.18	0.19	0.20	0.22	0.24	0.28	Total
No. of subjects	18	22	91	23	60	13	47	3	17	0	3	1	1	1	300
Per cent	13.3		84.7							2.0					100

During Normal Sinus Rhythm

P-R interval (sec.)	0.10	0.11	0.12	0.13	0.14	0.15	0.16	0.17	0.18	0.19	0.20	0.21	0.22	Total
No. of subjects	1	1	15	12	39	50	37	7	12	4	3	2	1	184
Per cent	1.1		93.5							5.4				100

in the P-R interval between normal sinus rhythm and atrial rhythm could be determined. In one-fifth of these records, there was no apparent change in the P-R interval associated with the P vector change (Fig. 3). In one-third, the P-R interval shortened by only 0.01 second. In over half, it shortened 0.02 second or less, and in 90 per cent of the cases, the P-R interval shortened 0.04 second or less.

The absolute length of the P-R interval associated with P wave inversion is of little importance in determining the exact location of the pacemaker because, in the majority of cases, the P-R interval is normal. It is the change in the P-R interval that is of special interest. In nearly all cases, there is shortening of the P-R interval, but the shorter the P-R interval while in normal sinus rhythm, the smaller will be the change in the P-R interval as the pacemaker shifts to a lower site.

In nineteen of the 172 electrocardiograms (in which the P-R interval during both atrial and normal sinus rhythm was available) the P-R interval was 0.10 to 0.12 second while in normal sinus rhythm. Thirteen of these records showed shortening of the P-R interval during atrial rhythm, but in no subject did the P-R interval shorten more than 0.02 second. In six of the nineteen cases, the P-R interval actually increased (Fig. 3). During the transition from normal sinus rhythm to atrial rhythm, in five out of the six cases it increased 0.01 and 0.02 second. In one case, it increased 0.12 second; the P-R interval was 0.16 second during normal sinus rhythm and 0.28 second during atrial rhythm.

Effect of Respiration, Body Position and Exercise: A characteristic feature of passive atrial rhythm is its intermittent character. One hundred seventeen (38 per cent) of the 328 subjects with atrial rhythm showed only retrograde atrial excitation and thus demonstrated a persistent

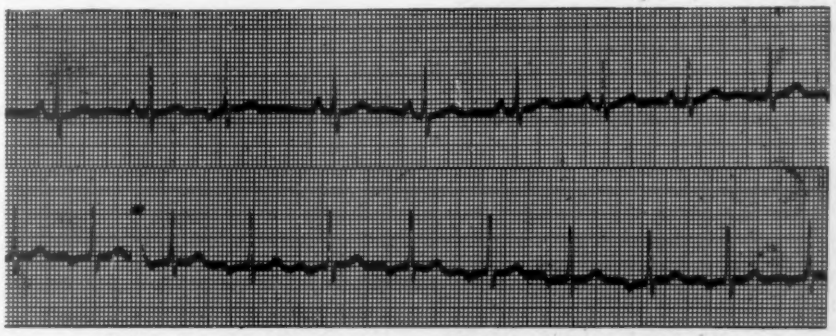


FIG. 3. Atrial rhythm. *Upper strip*, the P-R interval does not change appreciably when the atrial focus becomes the pacemaker. *Lower strip*, the P-R interval lengthens, suggesting increased delay at the A-V junction.

atrial rhythm. Special studies performed on forty-nine subjects in this laboratory and on forty-four subjects at other facilities demonstrated that only one subject showed persistent P wave inversion when subjected to various respiratory maneuvers, postural changes and exercise. In eight of thirty-eight subjects evaluated at their home bases and six of fifty-eight referred to the School of Aviation Medicine, atrial rhythm could not be reproduced. Atrial rhythm will not develop in a number of subjects when in the standing or sitting position, but will develop while the subject is lying down, either with respiratory maneuvers or spontaneously. In several subjects, atrial rhythm was demonstrated while they were in the horizontal position on the tilt table, but at a certain point in tilting them upright, normal sinus rhythm occurred. These findings suggest that permanent atrial rhythm is uncommon and that most subjects who demonstrate passive atrial rhythm can be converted to normal sinus rhythm.

In the ninety-three patients receiving special evaluation, it was observed that normal sinus rhythm was usually present after standing, exercise, intravenous administration of atropine or other procedures that would increase cardiac rate or decrease vagal tone. Atrial rhythm occurred most often when the subject was lying down, especially after deep inspiration. Normal sinus rhythm was often present immediately after standing; then, three or more minutes later, the heart rate would slow and atrial rhythm would occur. Some subjects did not show atrial rhythm with respiratory maneuvers while standing, but would while lying down. Less commonly, atrial rhythm occurred immediately on standing or during inspiration.

Incidence of Heart Disease: Of the ninety-three subjects receiving special evaluation, none had evidence of organic heart disease. None of these had abnormal double Master exercise tests. It was frequently observed that when atrial rhythm was present at the time of the exercise test, normal sinus rhythm was present after exercise. There did not appear to be any increased familial tendency toward coronary heart disease. Eight subjects gave a previous history of scarlet fever, but none were aware of previous rheumatic disease or rheumatic activity. In eight instances, the serum cholesterol level was over 300 mg. per cent. One subject was diagnosed at his home base as having familial hypercholesterolemia and had a serum cholesterol level of 425 mg. per cent. In one of the 328 subjects, aged twenty-four years, with atrial rhythm on a routine electrocardiogram, acute myocardial infarction subsequently developed.

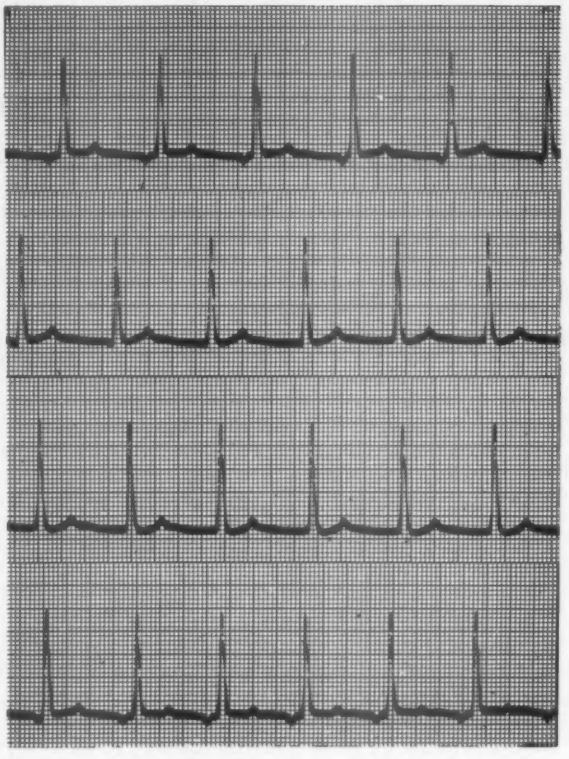


FIG. 4. A-V dissociation develops in the presence of atrial rhythm, with recapture occurring in the bottom strip.

Other Associated Arrhythmias: During evaluation, several subjects were found to have other arrhythmias. In several A-V dissociation developed while they were in atrial rhythm (Fig. 4). A-V dissociation was often initiated by a nodal escape beat. In one man an eight-second asystole developed during breath-holding following hyperventilation, and syncope resulted. He demonstrated upper nodal rhythm associated with a P-R interval of 0.08 to 0.09 second. In another subject normal sinus rhythm changed to A-V dissociation with breath-holding after hyperventilation, and he experienced symptoms of near-syncope. When given atropine intravenously, atrial rhythm developed followed by A-V dissociation and varying A-V block in the presence of atrial rhythm for eight minutes (Fig. 5). Administration of atropine abolished the symptoms of impending syncope induced by hyperventilation and breath-holding. In four subjects studied first degree A-V block de-

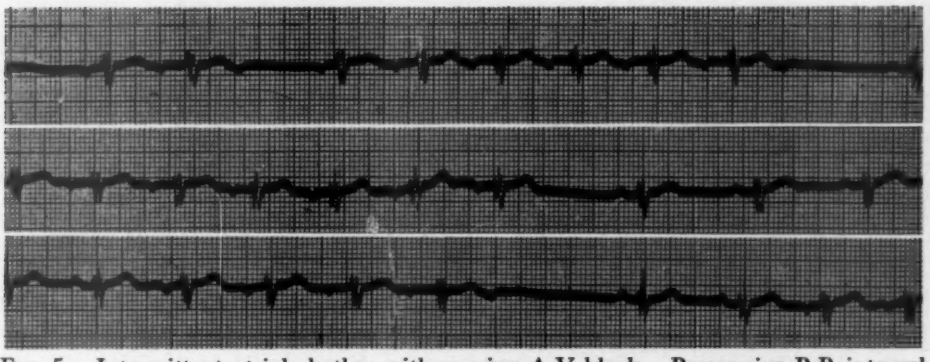


FIG. 5. Intermittent atrial rhythm with varying A-V block. Progressive P-R interval prolongation with a dropped beat is clearly demonstrated in the bottom strip.

veloped; two of them also had second degree A-V block.

Location of Ectopic Pacemaker: There is considerable disagreement among authorities concerning the location of the pacemaker when retrograde atrial excitation is present. The confusion began with the work of Zahn[3] and later, that of Meeks and Eyster.[4] Zahn classified the A-V node functionally into upper, middle and lower regions. He studied the node by warming various portions of it. These experiments were rather crude; later, Meeks and Eyster refined the study by measuring electrical impulses and by stimulating various regions of the heart and A-V node. These investigators thought they had confirmed the work of Zahn. It was concluded that the atria could not initiate impulses, and when the S-A node was not the pacemaker, the A-V node or other areas of specialized conductive tissues always became the pacemaker.

The A-V node is only 5 mm. in length and 2 to 3 mm. in diameter. Experimental technics designed to study its three individual parts require a degree of precision not apparent in the work of either Zahn or Meeks and Eyster.

Coronary Sinus Rhythm: This is the term used by Scherf[5–9] to identify arrhythmias with retrograde atrial excitation and relatively normal P-R intervals. He assumed that the area adjacent to the A-V node near the coronary sinus or the coronary nodal region was the pacemaker site. Scherf comments that warming the area of the coronary sinus with the right atrium open invariably causes middle nodal rhythm with no apparent P waves. If this is correct, the observations of Meeks and Eyster[4] in producing upper nodal rhythm with the heart open cannot be accepted.

Langendorf, Simon and Katz[10] state that coronary sinus rhythm results in upright P waves with a short P-R interval, usually less than 0.12 second. Since so-called upper nodal rhythm is defined as a short P-R interval of less than 0.12 second, they classify retrograde atrial excitation associated with normal P-R intervals as upper nodal rhythm with A-V block, which is the same as Scherf's coronary sinus rhythm. This concept originated with the report of a patient with a P-R interval of 0.21 to 0.22 second during sinus rhythm and 0.16 to 0.18 second during retrograde atrial excitation. Apparently no experimental observations have been carried out to support this concept. It is difficult to accept the concept that a pacemaker in the upper portion of the 5 mm. node has a distinct area of block below it in the same small conducting body. Retrograde atrial excitation associated with a P-R interval of 0.12 second or more occurred in more than 260 instances in this survey and it therefore seems illogical to assume that all these asymptomatic subjects have a primary focus in the A-V node and A-V block.

Present Concept of Atrial Rhythm: Since the work that was the basis for the upper, middle, lower nodal concept, a great deal of information has been obtained. It is now accepted that numerous areas of nodal fibers are scattered throughout the subendocardial tissue of the atria which are potential pacemakers for the heart.[11] Atrial premature contractions may originate from such foci. We have adopted the view that such a pacemaker in certain locations can induce retrograde atrial excitation followed by the normal delay at the A-V junction (or less commonly by prolonged delay at the A-V junction) resulting in a P-R interval of 0.12 second or greater. For these reasons, we have classified retrograde atrial activation with normal or relatively unchanged P-R intervals as atrial rhythm.

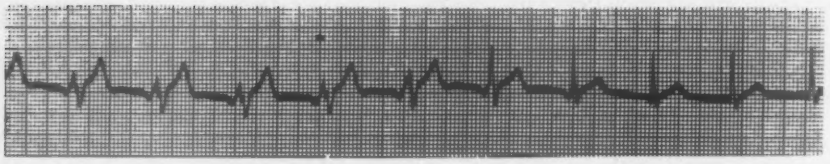


FIG. 6. Lead II recorded in a subject with the WPW syndrome. The QRS interval was more prolonged during atrial rhythm. When A-V dissociation occurred in the presence of atrial rhythm (seventh to tenth complexes) the QRS complex became normal.

Support for the concept of an atrial pacemaker without A-V block is found in four observations: (1) the high incidence of such an arrhythmia in young, healthy subjects; (2) the occurrence of typical atrial premature contractions with retrograde atrial excitation followed by an incomplete compensatory pause (implying that the S-A node was stimulated by the ectopic pacemaker); (3) A-V dissociation with retrograde atrial excitation and nodal control of the ventricles; and (4) failure of conversion of the WPW syndrome to normal ventricular conduction in the presence of retrograde atrial excitation.

It is more likely that A-V dissociation accompanied by retrograde atrial excitation results from dissociation between the atria and A-V node rather than from dissociation within the 5 mm. node between two nodal foci.

Since aberrant ventricular excitation in the WPW syndrome is dependent upon an accessory pathway between the atria and ventricles, it is highly significant that ventricular excitation returns to normal whenever A-V dissociation occurs. Persistence of ventricular pre-excitation during retrograde atrial excitation strongly suggests that the atria are in fact stimulated by an atrial focus rather than a nodal focus (Fig. 6). From an atrial focus, the accessory pathway can still function between the atria and ventricles but it cannot cause pre-excitation when the primary pacemaker is in the A-V node.

In view of these comments, we seriously question the concept of upper nodal rhythm with A-V block and assume that upper nodal rhythm is relatively rare. It is further assumed that retrograde atrial excitation occurs commonly in young, healthy subjects and is closely related to vagal tone. Such an atrial focus may be associated with variations in excitation, including a short, normal or prolonged P-R interval, or other forms of A-V block, aberrant ventricular excitation in the WPW syndrome and A-V dissociation. The term "upper nodal rhythm" should be restricted to those patients with P-R intervals of 0.10 second or less and many of these may, in fact, be shown to have atrial rhythms if compared to the P-R interval during normal sinus rhythm. The presence of retrograde atrial excitation is a common occurrence in young, healthy people and is not by itself a manifestation of cardiac disease or is it responsible for a significant disturbance in cardiovascular dynamics.

Active Atrial Rhythm: As a result of the electrocardiographic survey, seventeen subjects were classified as having active atrial rhythm. These included atrial rhythm initiated by an atrial premature contraction and atrial rhythm with a faster rate than the basic sinus rhythm. Included in this group were subjects who could be properly classified as having slow atrial tachycardia and repetitive atrial tachycardia. None of these subjects had clinical symptoms of paroxysmal tachycardia, since the cardiac rate was not excessive and the bursts of repetitive atrial tachycardia were short in duration.

Active atrial rhythm was often reproduced by exercise, standing, expiration or breath-holding (Fig. 7). It occurred with procedures that ordinarily increased the heart rate. This indicated that decrease in vagal tone resulting from these procedures allowed the more rapid ectopic focus in the atria to take over. Although there were a few exceptions, atrial premature contractions seldom occurred in the group with passive atrial rhythm. They were predominantly confined to those subjects who

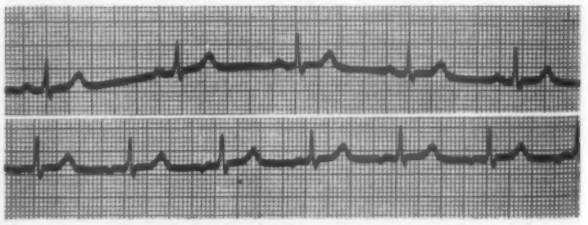


FIG. 7. Active atrial rhythm with a faster heart rate during atrial rhythm as compared to normal sinus rhythm (continuous strip).

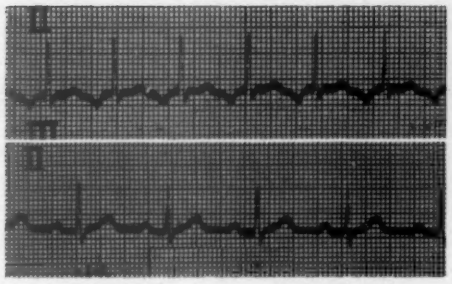


FIG. 8. Case 1. *Upper strip*, atrial tachycardia. *Lower strip*, normal sinus rhythm.

demonstrated an active atrial focus which served to initiate runs of active atrial rhythm.

Several examples of active atrial rhythm or repetitive atrial tachycardia were of sufficient interest to warrant further comment.

CASE 1. A thirty-five year old pilot was found to have persistent atrial tachycardia, rate 115 per minute, on a routine electrocardiogram. He was asymptomatic and the only significant past history was an irregularity of the pulse noted on annual physical examination at the age of twenty-four. During his evaluation, he varied intermittently between normal sinus rhythm and slow atrial tachycardia (Figs. 8 and 9). It was possible to convert the atrial tachycardia to normal sinus rhythm by carotid sinus massage and breath-holding. The P wave configuration was the same in the presence of isolated premature beats as noted during atrial tachycardia. Exercise and maneuvers that increased the cardiac rate resulted in atrial tachycardia. Maneuvers that increased vagal tone resulted in normal sinus rhythm. These observations indicate that an active atrial focus with an inherent rate of approximately 120 per minute was present and capable of assuming the role as the primary pacemaker whenever vagal tone was diminished.

CASE 2. A twenty-five year old officer was noted to have an abnormally rapid heart rate at the time of a routine physical examination. Thorough evaluation revealed no evidence of underlying heart disease. A routine electrocardiogram, however, disclosed a basically normal sinus rhythm with short bursts of atrial tachycardia at a rate of 150 per minute associated with episodes of A-V block (Fig. 10).

CASE 3. A twenty-five year old pilot was found to have repetitive atrial tachycardia initiated by premature atrial beats. When the ectopic atrial focus initiated the beat, the P-R interval was prolonged (Fig. 11). This is because the premature atrial discharge occurred during the relative refractory period for the A-V junction from the preceding cycle. The earlier the premature impulse, the greater would be the prolongation of the P-R interval. When the impulse was sufficiently early to fall within the absolute refractory phase for the preceding cycle, the

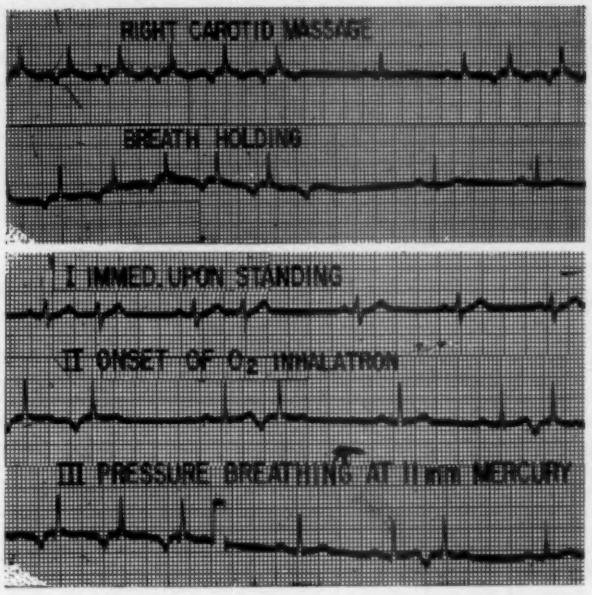


FIG. 9. Case 1. *Upper strips*, termination of atrial tachycardia with carotid sinus massage and breath-holding. *Lower strips*, examples of atrial premature beats on standing, inhalation of oxygen and pressure breathing.

atrial impulse was completely blocked. The apparent progressive prolongation of the P-R interval with actual blocked impulses presents a pseudo-Wenkebach phenomenon.

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

Of special interest were eight cases of paroxysmal supraventricular tachycardia among subjects on flying status. Several were combat veterans, and nearly all had been flying for at least ten years and had successfully passed numerous rigid physical examinations. In contrast to the preceding group, in which arrhythmia was detected as a result of a routine electrocardiogram, all eight subjects originally sought medical attention because of symptoms associated with a paroxysmal atrial tachycardia. Two of these cases occurred in association with the WPW syndrome.

The characteristic history in this group of subjects was that they had been fatigued, under emotional stress or had maintained poor personal hygiene. Most of the subjects who experienced several episodes learned themselves that vagal maneuvers such as breath-holding would abort their attacks. All patients except one were in the thirty to forty year age group. Only one subject demonstrated significant findings on special examinations; 2:1 atrial flutter developed while he was on the tilt table.

Supraventricular tachycardia without heart

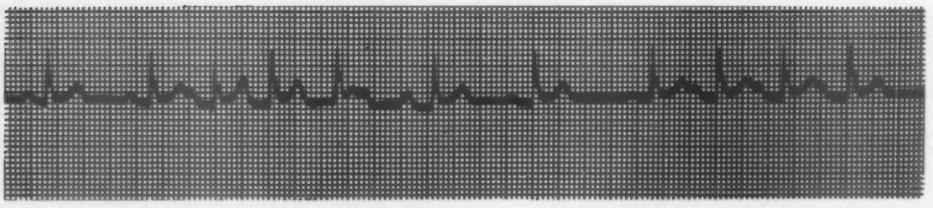


FIG. 10. Case 2. Short burst of atrial tachycardia with occasional blocked atrial impulse (following fifth QRS complex).

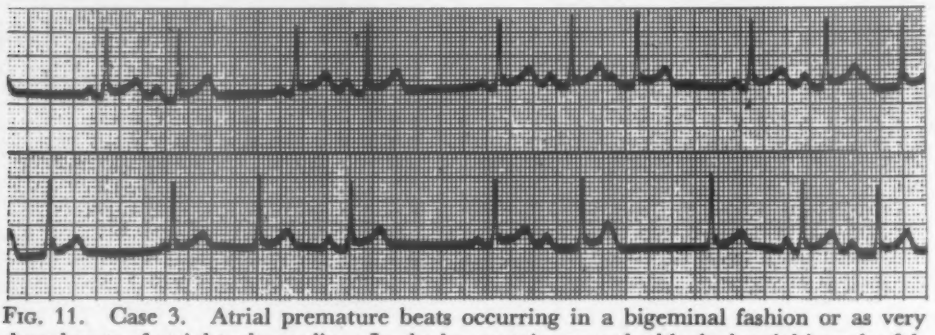


FIG. 11. Case 3. Atrial premature beats occurring in a bigeminal fashion or as very short bursts of atrial tachycardia. In the lower strip, note the blocked atrial impulse following the sixth QRS complex (P wave superimposed on T wave) followed by nodal escape.

disease is common.[12–15] Long term evaluation of several series of patients has shown that the occurrence of paroxysmal atrial tachycardia in apparently healthy persons seems to have no effect on prognosis or longevity.

ATRIAL FIBRILLATION

Five cases of atrial fibrillation were detected during the course of reviewing 67,375 records. None of these subjects had been previously diagnosed and all were on active Air Force flying duty. Their ages were twenty-two, twenty-eight, thirty-six, thirty-eight and forty-five years.

CASE 4. A thirty-six year old pilot was seen who had flown either as a civilian or in the Air Force for eighteen years. He had been in combat for three years and had flown fifty missions in World War II. On questioning, he admitted that he "always had difficulty taking his own pulse," because it seemed irregular, even during childhood. During the annual physical examination doctors frequently listened to his heart for a long time and would question him as to whether or not he had any type of heart disease. However, the patient had never experienced any symptoms, had played basketball in college and had always been very active physically. It was not until his first electrocardiogram was taken at the age of thirty-four that the diagnosis of atrial fibrillation was made. An exhaustive examination at the time failed to disclose the etiology of his atrial fibrillation. He has been followed up for over two years and chronic atrial fibrillation persists without symptoms or signs of other disease.

Atrial fibrillation occurs most commonly in rheumatic heart disease with mitral stenosis, coronary heart disease and hyperthyroidism. It is less commonly observed in asymptomatic subjects with apparently normal hearts. In these subjects, the arrhythmia was precipitated by some non-cardiac cause.

In 1926, Orgain, Wolff and White[16] first emphasized a benign atrial fibrillation in certain instances when they presented forty-nine patients with this finding without signs of cardiac disease.

In 1930, Fowler and Baldridge[17] reported on ten patients in whom atrial fibrillation appeared without evidence of heart disease. They believed that abdominal disease and alcohol were the most common exciting agents. Friedlander and Levine[18] state that purely functional atrial fibrillation without organic heart disease accounts for 5 to 6 per cent of atrial fibrillation. Tobacco, alcohol and other toxic factors may be the precipitating causes. In others, emotional stress, fatigue, violent exertion and acute gastrointestinal illness may be implicated. Atrial fibrillation associated with these conditions is usually paroxysmal in character and brief in duration.

NODAL RHYTHM

Of the 67,375 subjects in whom routine electrocardiograms were recorded, only nine demonstrated nodal rhythm. Three records demonstrated middle nodal rhythm with the P waves buried in the QRS complexes. In all records, the P-R interval was less than 0.10 second. All

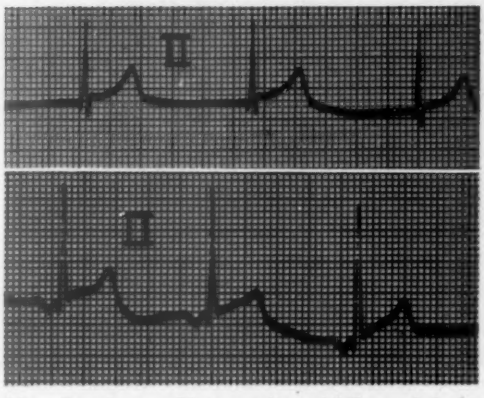


FIG. 12. Lead II. *Upper strip*, middle nodal rhythm. *Lower strip*, upper nodal rhythm.

but two were intermittent with the pacemaker changing from the S-A node to the A-V node during the course of a routine twelve-lead electrocardiogram. Six of the subjects had passive nodal rhythm evidenced by cardiac slowing as the pacemaker shifted to the A-V node (Fig. 12). The other three subjects had an active nodal focus intermittently controlling the heart, with repetitive nodal tachycardia. The rate while in nodal rhythm in these three records was 80, 95 and 120 per minute, respectively.

CASE 5. A thirty-seven year old pilot gave a history of a recent episode of unexplained loss of consciousness. He had no evidence of organic heart disease. When in a horizontal position on a tilt table, a persistent nodal rhythm with a P-R interval of 0.09 second and a cardiac rate of 62 per minute developed. With the subject tilted to the upright position, normal sinus rhythm appeared, but maneuvers designed to slow the heart would produce short periods of nodal rhythm.

The rarity of classic nodal rhythm in an asymptomatic healthy population is pointed up by the low incidence (0.01 per cent) noted in this survey. Even in the absence of cardiac disease the slow heart rate accompanying passive nodal rhythm is not infrequently associated with symptoms of syncope and tendency to collapse due to bradycardia.

SUPRAVENTRICULAR PREMATURE CONTRACTIONS

Supraventricular ectopic beats were noted in 329 records, comprising 12.9 per cent of the total abnormalities. This produced a rate of 4.9 per 1,000 subjects. There appeared to be no significant difference in the incidence of the supraventricular ectopic beats among the various age groups (Fig. 13). There were no other signs of cardiac disease.

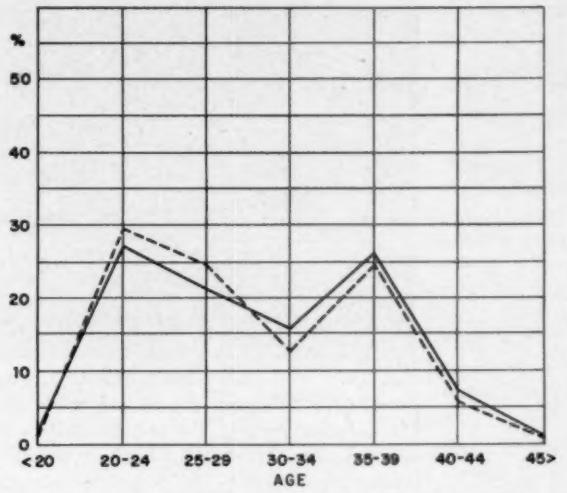


FIG. 13. Incidence of supraventricular contractions. The solid line depicts the per cent of the population surveyed in each five-year group. The broken line shows the per cent of all subjects with supraventricular premature contractions in each five-year age group. The similarity of the curves indicates that age is not a factor in the frequency of supraventricular premature contractions.

WANDERING PACEMAKER

One hundred fifty-two (0.22 per cent) were found to have a wandering pacemaker. None were included in the group with atrial rhythm. This term was applied to those subjects who had a gradual change in the location of the pacemaker in a cyclic fashion without the lower pacemaker establishing a basic rhythm. In

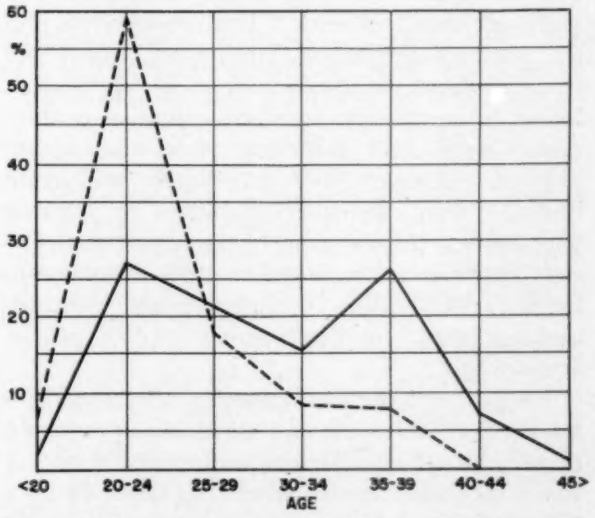


FIG. 14 Incidence of wandering pacemaker. The solid line depicts the per cent of the population surveyed in each five-year age group. The broken line shows the per cent of all subjects with wandering pacemaker in each five-year age group. The increase in frequency of subjects with wandering pacemaker in the younger age groups is apparent.

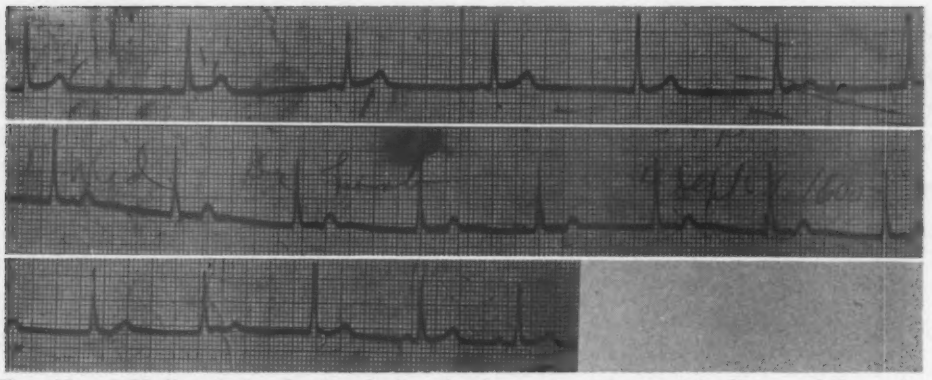


FIG. 15. A-V dissociation begins during the first strip. An upright P wave follows the sixth QRS complex due to S-A node stimulation. Lower nodal rhythm and retrograde P waves are seen in the second strip. Lower nodal rhythm changes to A-V dissociation again in the bottom strip with an upright P wave following the second QRS complex and finally recapture by the S-A node occurs.

two subjects the pacemaker was gradually displaced into the A-V node. The majority of subjects demonstrating this arrhythmia were in the younger age group. Sixty-five per cent were twenty-four years of age or younger while only twenty-nine per cent of the total survey were twenty-four years of age or younger (Fig. 14).

The preponderance of young subjects with this finding suggests that it is not associated with significant cardiac disease and is more closely related to vagal inhibition of cardiac excitation. Its significance is comparable to that of atrial rhythm.

A-V DISSOCIATION

A-V dissociation was found in thirty-three (0.05 per cent) subjects. The majority were in the younger age group, twenty-six (eighty per cent) of them twenty-four years of age or less. Six of these subjects received extensive evaluation. None had evidence of cardiovascular disease. In three, A-V dissociation was again induced with maneuvers designed to increase vagal tone. In the other three instances it was not possible to reproduce A-V dissociation. Subsequent tracings in many other instances demonstrated the intermittent nature of the arrhythmia.

For purposes of classification, all electrocardiograms that demonstrated dissociation between atrial and ventricular excitation for three or more successive cycles were diagnosed as A-V dissociation. Isolated escape beats with dissociation were not included in this category. In all instances, the atrial and ventricular rates were very similar. With relatively long continuous records, all examples of A-V dissociation proved to be intermittent in nature.

The incidence of A-V dissociation reported from hospital and clinic facilities is seven in 8,000 records and forty-eight in 10,000 records. It is reported to occur in acute rheumatic fever and other febrile illnesses. It may occur after digitalis administration. Marriott et al.[19] report it may occur secondary to variations in autonomic control of the heart such as during respiratory maneuvers, ocular pressure, carotid sinus pressure, the administration of atropine, increased intracranial pressure, pheochromocytoma and by administration of a variety of drugs. Marriott, however, states that A-V dissociation is seen predominantly in elderly patients with severe degenerative cardiovascular disease, since only six of his thirty-nine patients had no evidence of heart disease and nearly all were over fifty years of age. This is in sharp contrast to the observations of our survey in which A-V dissociation was most common in the younger age groups and demonstrable heart disease was not a factor.

Although A-V dissociation was relatively infrequent on routine electrocardiograms obtained with the subject recumbent, it should be pointed out that A-V dissociation is relatively common during respiratory maneuvers, orthostatic stress and administration of atropine.[20–22]

Even if heart disease can be satisfactorily excluded in these subjects, the question remains concerning the stability of cardiovascular dynamics in subjects with A-V dissociation observed on routine tracings. A-V dissociation is a form of nodal rhythm and is commonly associated with relative bradycardia. Many examples of induced syncope observed in this laboratory have been associated with A-V dissociation and cardiac arrest, often initiated

by simple respiratory maneuvers. The answer as to whether or not subjects with spontaneous A-V dissociation are in fact more prone to circulatory collapse awaits further investigation.

A-V dissociation is closely related to nodal rhythm as exemplified by several instances of A-V dissociation changing to lower nodal rhythm and back again to A-V dissociation (Fig. 15).

SINUS ARREST

Five examples of sinus arrest with escape beats were noted. None of the periods of arrest were prolonged. In four instances a nodal escape beat terminated the transitory arrest and in one instance the escape beat originated from an atrial focus. All were noted in young people, their ages being twenty to twenty-four years. Sinus arrhythmia and sinus bradycardia (rate 50 to 60 per minute) was a feature of all. Short transitory sinus arrest with a very early escape beat has no apparent ill effects on cardiovascular dynamics and is not apparently associated with heart disease. Most likely such innocuous findings are due to increased vagal tone, so common in the younger age group.

Summary

Of 67,375 healthy members of the Air Force flying population, 861 subjects had supraventricular arrhythmias discovered by a routine electrocardiogram. These included 328 subjects with atrial rhythm, 329 with supraventricular premature contractions, 158 with wandering pacemaker, thirty-three with A-V dissociation, nine with nodal rhythm, five with atrial fibrillation, and five with sinus arrest with nodal escape.

Increased vagal tone, common to youth, appears to be the greatest cause of atrial rhythm (sometimes called upper nodal rhythm with A-V block), wandering pacemaker, sinus arrest with nodal escape, A-V dissociation and perhaps nodal rhythm. A high incidence of these abnormalities occurs below the age of twenty-five years and the incidence drops sharply past this age. This is in contradistinction to premature contractions which occur at the same rate per thousand subjects through all age groups of the survey.

References

1. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1,000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
2. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force air crew. *Circulation*, 10: 401, 1954.
3. Zahn, A. Experimentelle Untersuchungen uber Reizbeldung und Reizleitung in Atrioventrikularknoten. *Arch. ges. Physiol.*, 151: 247, 1913.
4. Meeks, W. J. and Eyster, J. A. E. Experiments on the origin and propagation of the impulse in the heart. III. The effect of vagal stimulation on the location of the pacemaker in auriculo-ventricular rhythm, and the effect of vagal stimulation on this rhythm. *Heart*, 5: 227, 1913.
5. Scherf, D. Upper auriculo-ventricular rhythm (coronary sinus rhythm) experimentally produced. *Proc. Soc. Exper. Biol. & Med.*, 56: 220, 1944.
6. Scherf, D. and Harris, R. Coronary sinus rhythm. *Am. Heart J.*, 32: 443, 1946.
7. Scherf, D. and Schott, A. Extrasystoles and Allied Arrhythmias, p. 71. New York, 1953. Grune & Stratton.
8. Scherf, D. The atrial arrhythmias. *New England J. Med.*, 252: 928, 1955.
9. Scherf, D. and Gurbuzer, B. Further studies on coronary sinus rhythm. *Am. J. Cardiol.*, 1: 579, 1958.
10. Langendorf, R., Simon, A. J. and Katz, L. N. A-V block in A-V nodal rhythm. *Am. Heart J.*, 27: 209, 1944.
11. Katz, L. N. and Pick, A. Clinical Electrocardiography. The Arrhythmias, p. 19. Philadelphia, 1956. Lea & Febiger.
12. Parkinson, J. and Papp, C. Repetitive paroxysmal tachycardia. *Brit. Heart J.*, 9: 241, 1947.
13. Wedd, A. M. and Wilson, D. C. Standstill of the heart of vagal origin. *Am. Heart J.*, 5: 493, 1930.
14. Campbell, M. and Elliot, G. A. Paroxysmal tachycardia; etiology and prognosis of 100 cases. *Brit. Heart J.*, 1: 123, 1939.
15. Cooke, W. T. and White, P. D. Prognosis of paroxysmal tachycardia and paroxysmal auricular fibrillation. *Brit. Heart J.*, 4: 153, 1942.
16. Orgain, E. S., Wolff, L. and White, P. D. Uncomplicated auricular fibrillation and auricular flutter. Frequent occurrence and good prognosis in patients without other evidence of cardiac disease. *Arch. Int. Med.*, 57: 493, 1926.
17. Fowler, W. M. and Baldridge, C. W. Auricular fibrillation as the only manifestation of heart disease. *Am. Heart J.*, 6: 183, 1930.
18. Friedlander, R. D. and Levine, S. A. Auricular fibrillation and flutter without evidence of organic heart disease. *New England J. Med.*, 211: 624, 1934.
19. Marriott, H. J. L., Schubert, A. F. and Bradley, S. M. A-V dissociation: a reappraisal. *Am. J. Cardiol.*, 2: 586, 1958.
20. Lamb, L. E., Dermksian, G. and Sarnoff, C. A. Significant cardiac arrhythmias induced by common respiratory maneuvers. *Am. J. Cardiol.*, 2: 563, 1958.
21. Dermksian, G. and Lamb, L. E. Cardiac arrhythmias in experimental syncope. *J. A. M. A.*, 168: 1628, 1958.
22. Averill, K. H. and Lamb, L. E. Less commonly recognized actions of atropine on cardiac rhythm. *Am. J. M. Sc.*, 237: 304, 1959.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

III. Ventricular Rhythms*

CAPT. ROLAND G. HISS, MC, USAF, CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THIS paper presents the incidence of various ventricular rhythms found in an electrocardiographic survey of 67,375 healthy male subjects of various ages.

A ventricular rhythm may be defined as a period of cardiac excitation where the dominant pacemaker is located somewhere in the ventricular system. The types of ventricular rhythms span a wide range of cardiac arrhythmias from innocuous premature ventricular contractions to ventricular tachycardia and ventricular fibrillation. There is little known of the incidence of these arrhythmias in the asymptomatic healthy population.

MATERIAL AND METHODS

The population of this survey was composed of 67,375 male subjects on flying status with the U. S. Air Force. All these men were, to the best of our knowledge, asymptomatic. They received fairly close medical observation through annual routine physical examinations and readily available medical attention from their flight surgeons and other Air Force medical facilities. Electrocardiograms were obtained solely for the purpose of fulfilling the Air Force regulation which requires a baseline electrocardiogram on all members of the flying population; records taken because of clinical indication have been excluded. The details of this survey have been described in the first paper of this series.[1]

An analysis was made of the age incidence and associated heart rates of those subjects who demonstrated one or more premature contractions which were indisputably of ventricular origin. In each case an attempt was made to localize the site of the ectopic focus either to the right or to the left ventricle. It is admitted that it is not possible to do this with assurance in all cases.

Premature ventricular systoles of parasystolic origin were interpreted differently from the isolated premature ventricular contractions bearing a fixed relationship to the preceding normal beat. Ventricular tachycardia and three cases of idioventricular rhythm with A-V dissociation were detected and investigated. An additional case of idioventricular rhythm from the flying population studied prior to this survey is reported since such findings are relatively rare.

RESULTS

Analysis of the records has revealed the presence of all known ventricular rhythms with the exception of ventricular flutter and ventricular fibrillation. As the ages of the subjects range from the late teens to the mid-fifties, it would seem justifiable to conclude that the incidence of various types of ventricular arrhythmias in the groups surveyed would be an approximate index of the incidence of these same arrhythmias in the entire asymptomatic, healthy adult population. The only exception which might be made stems from the fact that the entire population surveyed was male, and therefore any electrocardiographic entity which has sex preponderance would not be correctly assessed by this study. Clinically unrecognized arteriosclerosis and its various manifestations would be the only major diagnostic entity known to have definite preponderance for one sex which could be expected to distort these statistics. However, the various electrocardiographic phenomena discussed in this paper are not usually manifestations of arteriosclerosis (with the possible exception of the one example of multifocal pre-

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

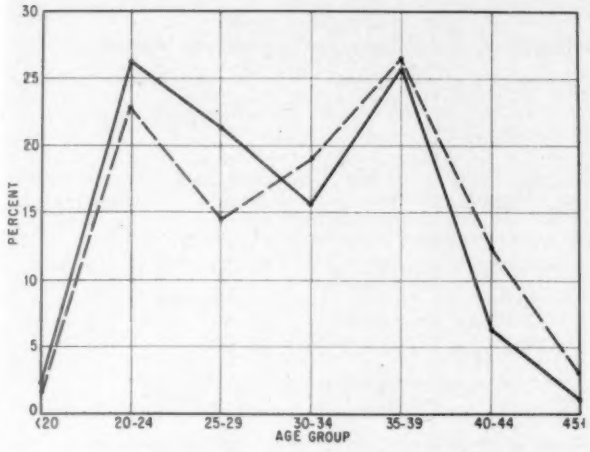


FIG. 1. The frequency distribution of ventricular premature contractions (broken line) compared with the entire survey population showed a slight increase in the older age groups. Values are expressed in per cent of respective population in each five-year age group.

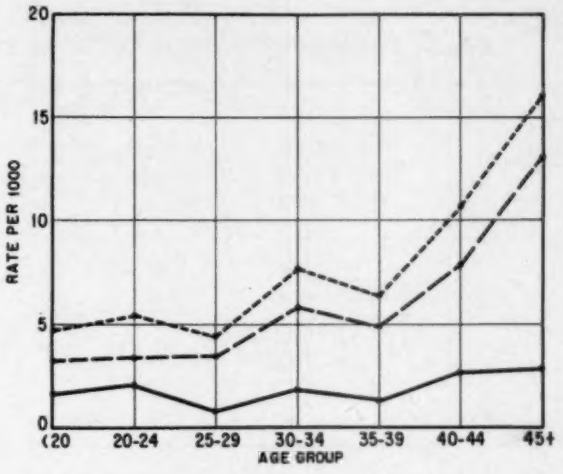


FIG. 2. The small broken line shows the rate per 1,000 incidence of premature ventricular contractions. The rates of premature contractions originating in the right ventricle (large broken line) and in the left ventricle (solid line) indicate a marked increase of the former but no change of the latter in the older age groups.

mature ventricular contractions and the one instance of ventricular tachycardia).

If it is assumed that this study provides a reliable index of ventricular rhythms in the normal, healthy population (the size of the population surveyed lends definite statistical significance), it may be concluded that the incidence of various ventricular rhythms in a healthy population is actually quite low.

ISOLATED PREMATURE VENTRICULAR CONTRACTIONS

Of the 67,375 subjects surveyed, 419 (0.62 per cent) showed one or more isolated premature ventricular contractions. The average age of these subjects was 31.8 years, which is not significantly different from the average age of the entire survey group. The average heart rate was 71.4 beats per minute, which also is approximately the same as the average heart rate on all tracings.

A comparison of the frequency distribution of subjects in each five-year age group from the population surveyed and the frequency distribution of subjects in each five-year age group with ventricular premature beats demonstrates a significant increase in the incidence of this abnormality in subjects more than forty years of age (Fig. 1). Expressed in another manner, the rate per 1,000 varied between 4.7 and 7.7 between sixteen and thirty-nine years of age; 10.7 between forty to forty-four years; and 16.1 above forty-five years of age (Fig. 2).

The number of subjects showing ventricular premature beats (419 or 0.6 per cent) was considerably smaller than had been expected. It has long been recognized that few people live a lifetime without an occasional premature ventricular contraction, but the probability that a chance prematurity occurred during the brief duration of a routine electrocardiogram is quite small. It is believed that most of the 419 subjects who showed premature ventricular contractions were those who have premature beats rather frequently.

The medical literature provides a wide range of other incidence values for ventricular premature beats. Scherf and Schott[2] have summarized most of these and point out that the incidence in a given survey will depend on the age of the population studied and the clinical status of its members. Thus, White found 974 (9.7 per cent) patients with premature ventricular beats in 10,000 who had electrocardiograms at the Massachusetts General Hospital from 1914 to 1931,[3] and 2,007 (8 per cent) of 25,000 from 1934 to 1943.[4] Katz and Pick[5] found 3,745 instances of ventricular premature beats in their series of electrocardiograms on 50,000 patients. As these last three studies were conducted on hospital and office patients (many of them with heart disease), their results cannot be compared to ours. Studying asymptomatic subjects, Graybiel et al.[6] discovered eight (0.8 per cent) subjects with ventricular prematurities in a survey of 1,000 healthy young aviators, and Stewart and Manning[7] found nine (1.8 per cent) of 500 in their study of Royal

TABLE I
Relative Frequency of Premature Ventricular Contractions Originating from Right and Left Ventricles

Group	Premature Ventricular Contractions (no.)	Right Ventricle			Left Ventricle		
		Total No.	Average Age (yr.)	Average Rate (per min.)	Total No.	Average Age (yr.)	Average Rate (per min.)
I	1	103	32.51	69.79	44	31.30	69.34
II	2 to 4	111	32.10	71.87	45	30.13	69.87
III	5 to 10	53	33.87	72.85	18	27.58	75.44
IV	More than 10	41	30.79	74.27	4	34.00	68.75
Total	...	308	32.37	73.38	111	30.32	70.52

Canadian Air Force aircrew members. Dauwe[8] reports 141 instances (0.6 per cent) in 24,000 "normal subjects." By pooling all these studies with ours, of 92,875 people surveyed, there would be 577 (0.62 per cent) asymptomatic healthy subjects frequently showing ventricular premature beats. This incidence figure can be assumed to be approximately correct considering the size of the composite survey and the relative agreement of the contributing statistics.

The number of premature beats noted on the various tracings were divided into four groups as follows: group I, only one premature beat noted on the entire record; group II, two to four prematurities noted; group III, five to ten prematurities noted; and group IV, more than ten prematurities noted. Table I gives the age incidence and average heart rates of each of these four groups and also divides the total number of premature beats into two general types, those from the right ventricle and those from the left ventricle, respectively.

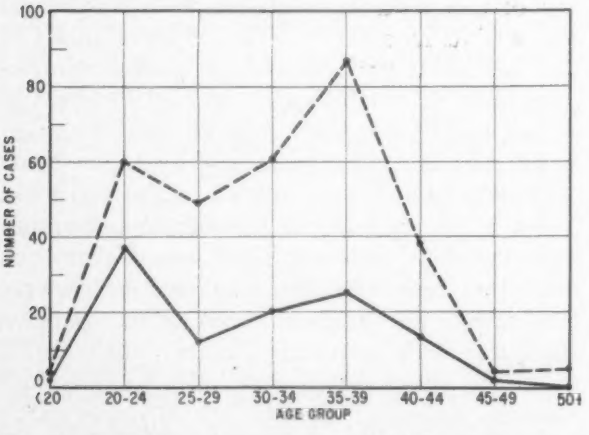


FIG. 3. Incidence of premature ventricular contractions originating from a focus in the right ventricle (broken line) as compared with those originating in the left ventricle (solid line) shows the total number of the former was approximately three times that of the latter.

The mounted electrocardiogram utilized in our survey included all twelve leads, each one approximately 4 cm. in length. Thus, forty-eight seconds of cardiac function were graphically recorded. As indicated in Table I, the average heart rate was approximately 71 beats per minute, so that a forty-eight–second record would average fifty-seven cardiac cycles. Thus, subjects with one premature beat on their record had one premature beat in fifty-seven beats (1.8 per cent). Subjects in the second group with two to four premature beats had three for every fifty-seven cardiac contractions (5.3 per cent). Those in the third group with five to ten premature beats averaged seven for every fifty-seven heart beats (12.3 per cent), and the last group with ten or more premature beats per tracing had at least ten for every fifty-seven beats (18 per cent). Table I shows that differences in heart rate do not account for the frequency of premature beats in the four groups.

Table I and Figure 3 show the age incidence of those subjects with ventricular premature beats from an ectopic focus in the right ventricle (QRS configuration similar to left bundle branch block) as compared with the left ventricle (configuration of right bundle branch block). The number of premature beats from the right ventricle was approximately three times those from the left ventricle; the rate per 1,000 incidence of the former increased fourfold from the youngest to the oldest age group while the rate per 1,000 of the latter did not change significantly (Fig. 2). Heart rates for both groups were the same.

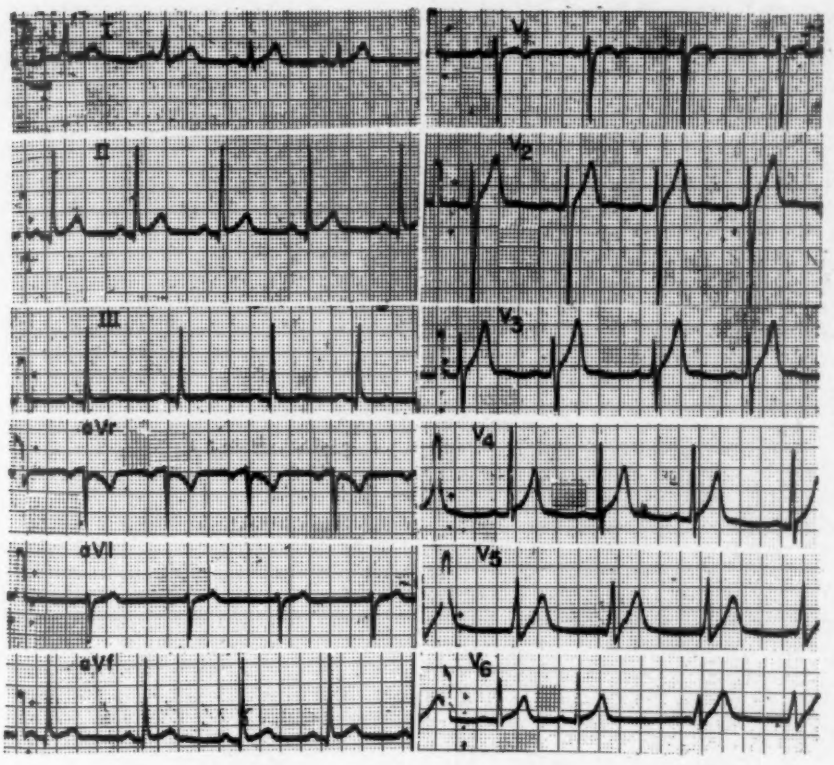


FIG. 4. Case 1. An example of A-V dissociation in which the lower focus was located within the ventricle. Note the first two complexes in lead I in which the superimposition of the P wave on the ascending limb of a widened QRS complex mimics the WPW syndrome. Examples of the idioventricular focus with absent P waves are seen in leads V_5 and V_6.

Of the 419 subjects who showed at least one premature ventricular contraction twenty-two (5.2 per cent) showed interpolated premature beats. These were evenly distributed through all age groups. There were sixteen which appeared to come from the right, and six from the left ventricle, which is approximately the same ratio as for all types of premature beats.

Rhythmically recurring premature beats producing the pattern of bigeminy, trigeminy or quadrigeminy were also noted to occur occasionally as follows: bigeminy, four cases (0.9 per cent of all premature beats); trigeminy, three cases (0.7 per cent); and quadrigeminy, one case (0.2 per cent). These variations arose from foci in the right vs. the left ventricle in the same ratio as for all premature beats, namely, 3 to 1. The incidence of bigeminy, trigeminy and quadrigeminy in the total population surveyed is exceedingly small. The percentages have not been calculated as the quantitative expression of such small numbers has doubtful significance. (Fusion beats from a supraventricular and a ventricular focus were seen in several cases, but this was considered *prima facie* evidence of ventricular parasystole and they are not included in this part of the study.)

There was only one instance in which the presence of *multifocal premature contractions* could be definitely ascertained. In all other cases the fixation of coupling was so constant and the configuration of premature beats within a given record was so similar that the diagnosis of multifocal ectopic beats could not be considered. This tends to support the generally accepted principle that multifocal premature ventricular contractions are evidence of organic heart disease.

A-V DISSOCIATION WITH IDIOVENTRICULAR RHYTHM

Three instances of true idioventricular rhythm with A-V dissociation were discovered. The definition of an idioventricular rhythm, in the broad sense, could include all forms of arrhythmia where a dominant ventricular focus is in control of the heart for three or more consecutive beats. (Two consecutive beats which are of ventricular origin may indeed arise from a ventricular focus and thereby be considered a

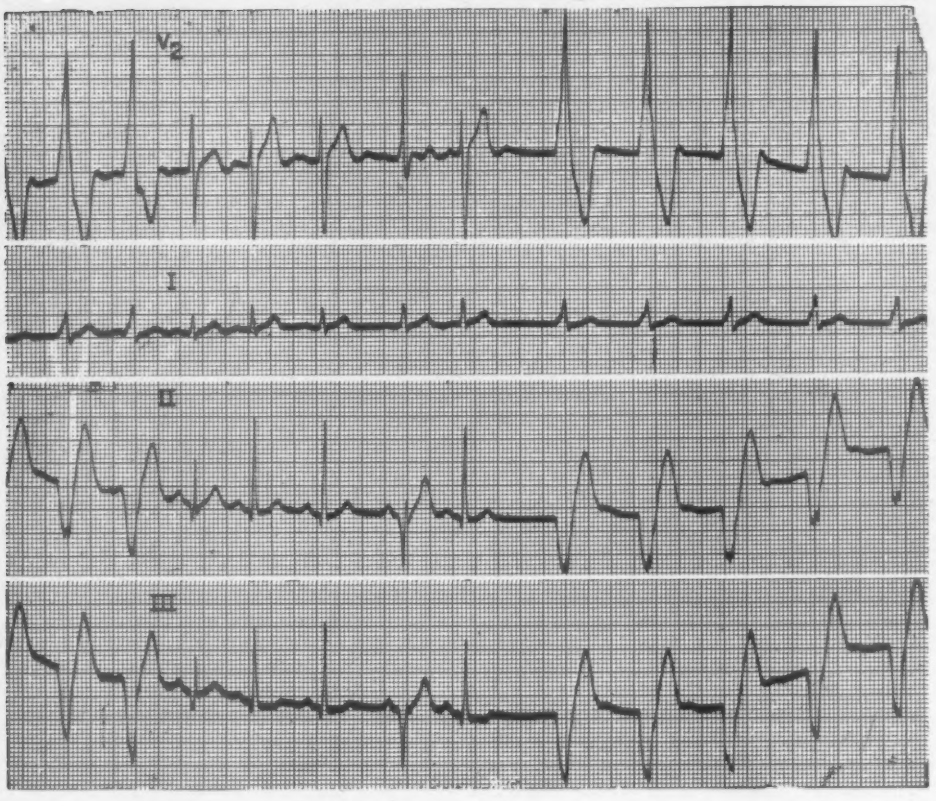


FIG. 5. Case 1. The first and last portions of the strip show A-V dissociation with an idioventricular focus in control of the heart. The middle portion shows ventricular capture by the sinus node with a fusion beat from the two foci seen in the sixth complex from the left. The four leads were recorded simultaneously.

short burst of idioventricular rhythm, but in most instances these prove to be simple premature beats with a double re-entry phenomenon.) The category of idioventricular rhythm could then include (1) ventricular parasystole in which exit block is not operative; (2) ventricular premature beats with successive repetitive re-entries; (3) ventricular tachycardia from an active ectopic ventricular focus; or (4) a ventricular rhythm originating from a focus somewhere in the ventricular conduction system acting as a reserve pacemaker. This latter variety is not pathologic and usually not active, but is the last unit in a chain of reserve pacemakers with which the heart is endowed. All three examples classified as idioventricular rhythm in this survey were of this type. They may simply be described as A-V dissociation with the ventricle being stimulated by a focus within the ventricle or below the main stem of the A-V node. Ventricular excitation resulted in broad QRS complexes as seen in ventricular premature beats or bundle branch block. In each case the basic rate of the idioventricular focus was very slow. Such rhythms in man are quite rare. None of the three subjects from the survey or the additional subject included in this report manifested any degree of A-V block.

The S-A node is the usual cardiac pacemaker, but in its temporary failure cardiac excitation may be passively assumed by a focus in the atria, the A-V node, the main stem bundle, either bundle branch or somewhere in the Purkinje system. These foci are believed to be physiologic and are always ready to fulfill the role of cardiac pacemaker should the focus above it in the chain temporarily fail to fire. The inherent rate of each is slower than the one above it, with the sinus node most rapid. Its action suppresses the others so that they are only seen intermittently and rarely in the normal subject. It would follow that the incidence of manifest reserve pacemakers would decrease in relation to their decreasing inherent rate. This has been our experience.[9] Atrial rhythm (the second fastest pacemaker in the heart) was seen in 328 subjects; nodal rhythm was seen in nine subjects and A-V dissociation with idioventricular rhythm was seen in only three subjects. A-V dissociation with an A-V nodal pacemaker was

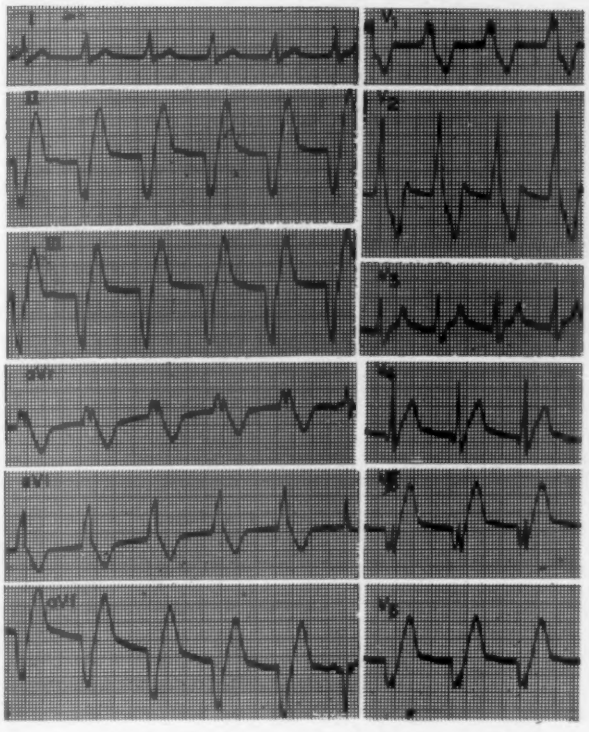


FIG. 6. Case 1. Routine twelve-lead electrocardiogram showing A-V dissociation with an idioventricular focus in control of the heart for almost every beat. Note the P wave immediately following the QRS complex in the third beat from the left of lead I, and the variable P-R interval in lead V_1. A fusion beat from the supraventricular and ventricular foci is seen in the last complex in leads aVR, aVL and aVF which were simultaneously recorded.

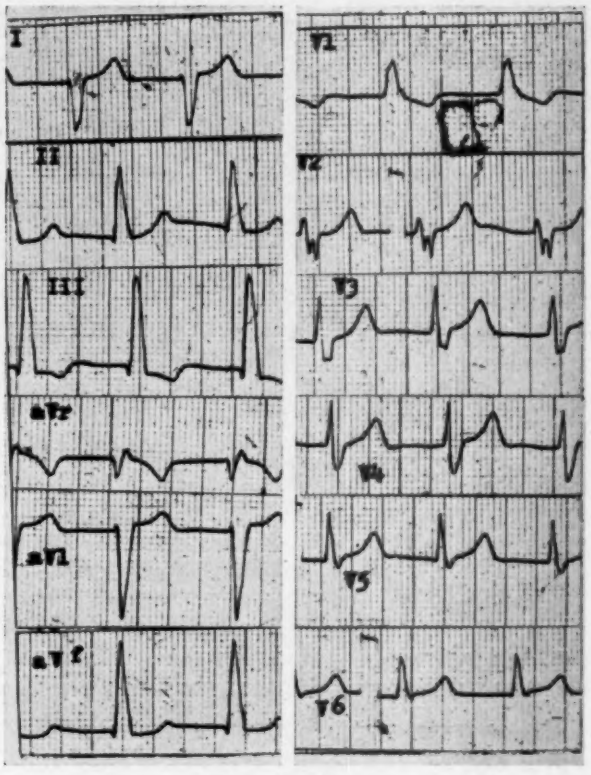


FIG. 7. Case 2. An idioventricular focus in the left bundle branch or left ventricle is in control of the heart throughout this routine tracing. Note the QRS configuration which mimics right bundle branch block and the absence of P waves.

seen in thirty-three subjects (ten times as often as A-V dissociation with an idioventricular pacemaker).

These three cases were of such unusual interest and extreme rarity as to warrant presentation as brief case histories. In each the function of pacemaker was intermittently assumed by some focus below the bifurcation of the A-V node when the normal sinus pacemaker was temporarily slowed. It may be assumed that the ventricular foci in these three subjects were considerably more active than would be expected. This is evidenced by their extreme readiness to become the cardiac pacemaker at the slightest slowing of the S-A nodal rate before an atrial or A-V nodal focus could assume control.

Each case may be regarded as a form of parasystole in the same sense that the A-V node is parasystolic to the S-A node. They are not, however, parasystole in the usual connotation by which is implied a focus in the ventricular muscle mass with its own inherent rate, entrance and exit block. This will be discussed later.

CASE 1. This was a twenty-four year old pilot whose routine electrocardiogram is shown in Figure 4. The first two ventricular complexes in lead I suggested an intermittent WPW syndrome and he was brought to the School of Aviation Medicine for further evaluation of the finding. Past medical and family histories were non-contributory. System review, physical examination, routine laboratory studies and roentgenogram of the chest were all within normal limits. A routine electrocardiogram was normal. However, with special maneuvers such as orthostasis, prolonged breath-holding, hyperventilation and deep rhythmic breathing, several episodes of A-V dissociation with an idioventricular focus acting as the lower pacemaker were intermittently observed (Fig. 5). These were most commonly observed during periods when the sinus pacemaker activity was slightly slowed, such as at the height of deep inspiration, following the release of prolonged breath-holding and after extended recumbency.

With exercise, such as following the double Master test, the heart rate increased to 105 beats per minute and a normal sinus rhythm prevailed. The rapid heart rate associated with hyperventilation was also of the normal sinus variety. It was only when the heart rate was slowed by some vagal mechanism that A-V dissociation was noted. Figure 6 shows a

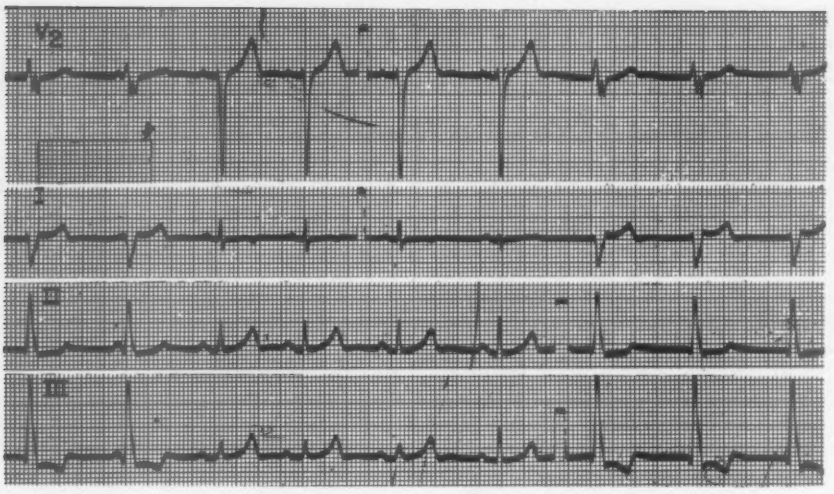


FIG. 8. Case 2. The four leads were recorded simultaneously. The first and last portions of the strip show A-V dissociation with an idioventricular focus as the subatrial pacemaker. The middle portion shows ventricular capture by the sinus pacemaker with normal sinus rhythm.

complete twelve-lead tracing with almost all beats of idioventricular origin.

Comment: It will be noted in Figure 4 that P waves can be seen immediately preceding some QRS complexes and superimposed on the ascending limb of the R wave (leads I, V_5 and V_6). It was this configuration which gave the initial erroneous impression of WPW syndrome. However, on closer examination, it was determined that the patient was demonstrating intermittent A-V dissociation with a ventricular focus below the A-V node, and ventricular fusion beats. Figure 5 demonstrates one example of an intermediary type configuration which is believed to be a fusion beat. This is the sixth complex from the left. In such cases, the ventricle may be excited at the onset of A-V dissociation by impulses originating from the atria as well as impulses originating from the ventricle. This results in a ventricular fusion beat resembling a WPW complex. This frequently occurs also when the atrial rate increases and just before atrial recapture occurs. Ventricular fusion beats cannot occur unless a focus below the bifurcation of the A-V node participates in excitation; therefore, fusion beats are not seen in A-V dissociation with the common A-V node acting as a pacemaker. Ventricular fusion beats do not occur in complete A-V block either since the atrial impulse cannot invade the ventricle.

CASE 2. This subject was a thirty-three year old pilot whose routine electrocardiogram is shown in Figure 7. During special maneuvers many examples of A-V dissociation with an idioventricular pacemaker were noted (Fig. 8). At the beginning of this tracing there is a ventricular pacemaker and no P waves are seen. The second complex in the tracing shows a P wave immediately in front of the QRS complex and the mid-portion of the tracing shows recapture of the ventricles by the S-A node with four sinus beats before dissociation again occurs. (It may be noted that while the ventricular focus is in control of the heart, the QRS complexes mimic the configuration of right bundle branch block, so that it may be postulated that the focus in question is located within the left bundle.)

Following intravenous injection of 1.2 mg. atropine sulfate, A-V dissociation was again noted (Fig. 9), but it was of a different type than formerly seen. This was the usual type of dissociation due to administration of atropine where the lower focus is nodal in location.

Comment: This subject showed two types of A-V dissociation. Without medication, maneuvers which elicit vagal responses and slow the heart caused A-V dissociation in which the lower focus was ventricular. It is postulated that the sinus rate fell below the inherent rate of the reserve ventricular pacemaker so that the latter assumed control of the heart in a passive manner. With administration of atropine, another form of A-V dissociation occurred, the A-V node being the lower focus in this case. A-V dissociation following administration of atropine is a common phenomenon in many normal subjects.[10] In this instance, release of vagal inhibition of the A-V node due to the action of atropine induced an active A-V dissociation

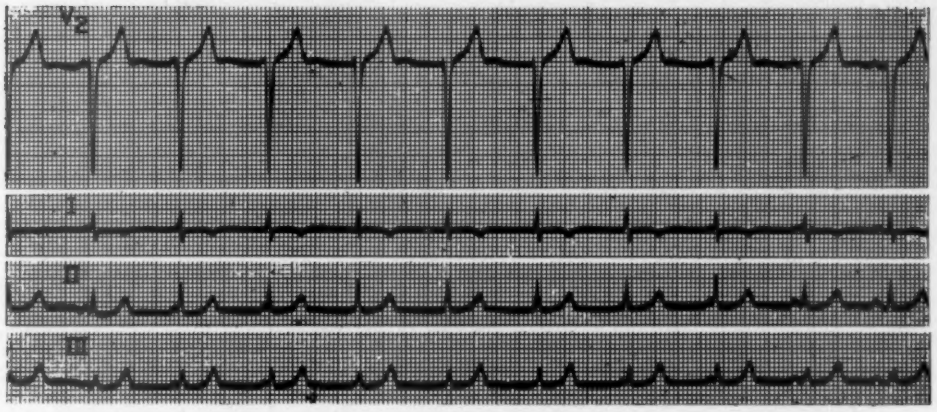


FIG. 9. Case 2. A-V dissociation occurred following intravenous injection of 1.2 mg. atropine sulfate. Note that the subatrial focus in this instance is located in the A-V node, producing QRS complexes which are normal in configuration. Compare the A-V dissociation seen in this figure with that in Figure 8 from the same subject.

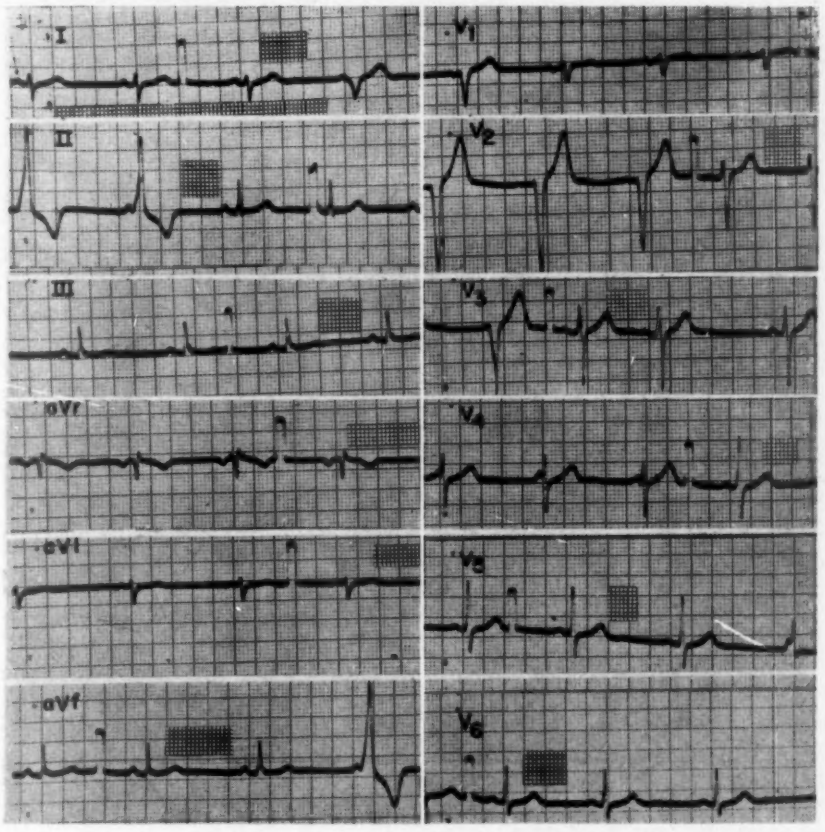


FIG. 10. Case 3. Routine tracing showing numerous episodes of transient A-V dissociation with an idioventricular focus in control of the heart. Ventricular capture by the sinus pacemaker is seen in leads II and V_2, and beginning dissociation with an idioventricular pacemaker in control is seen in leads aVF and V_5.

with the A-V nodal rate being faster than either the S-A nodal rate or the ventricular focus.

CASE 3. A thirty-seven year old man was without symptoms or other cardiac findings. His routine electrocardiogram (Fig. 10) showed transient, intermittent A-V dissociation with the lower focus being of ventricular origin. The first complex of lead II is a ventricular complex not associated with any P wave; the second complex has an upright P wave immediately preceding the bizarre QRS complex; the third complex is normal in character with a normal P wave and P-R interval. This is recapture of the ventricles by the normal sinus pacemaker, a phenomenon commonly observed during ordinary A-V dissociation where the nodal focus is the lower

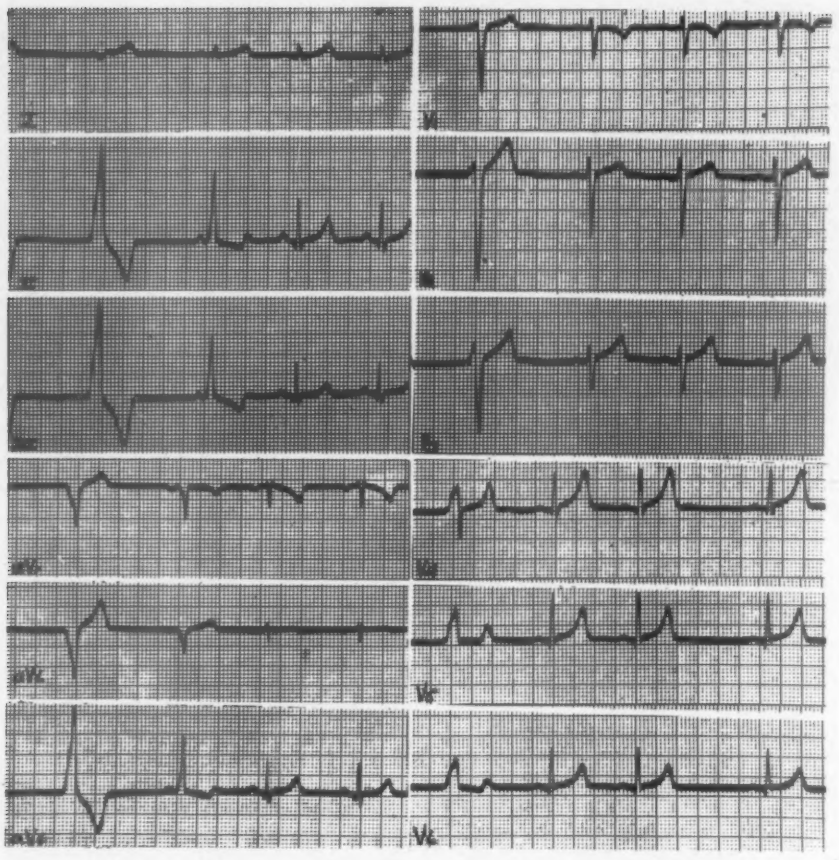


FIG. 11. Case 4. Numerous examples of transitory A-V dissociation between the sinus node and an idioventricular pacemaker are seen.

one, but only rarely seen with a ventricular focus acting as the faster, intermittently dominant, lower pacemaker. Special evaluation in this case demonstrated many intermediate types of fusion beats as well as runs of intermittent A-V dissociation with idioventricular rhythm.

CASE 4. The routine electrocardiogram of a forty-four year old pilot (Fig. 11) showed numerous fusion beats from the S-A node and a ventricular focus. This subject was not included in the statistics of the survey since his records were discovered by routine electrocardiogram prior to the survey. The recumbent electrocardiogram showed a variety of parasystolic-like fusion beats occurring singly, and with continuous electrocardiographic recording episodes of nodal rhythm were noted. The nodal focus at times shifted to the right main bundle, creating complexes resembling left bundle branch block (Fig. 12). On some occasions the timing of the nodal beats gave the appearance of simple nodal premature beats, whereas at other times the long delay before their occurrence gave the appearance of sinus arrest with nodal escape. Occasional superimposition of a sinus P wave on the initial limb of the widened QRS complex gave an impression of the WPW type complex (Fig. 13). This, on closer examination, proved to be fusion beats from the sinus and ventricular foci and dissociation of these two foci, with the ventricular focus the faster.

Comment: This is another example of physiologic cardiac pacemakers in action. With slowing of the S-A node, the inherent rate of a lower focus is reached and it became manifest. Two pacemakers are operative: the upper controls the atria, the lower and faster runs the ventricles; that is, by definition, A-V dissociation. In this subject, the subatrial focus was sometimes located in the A-V node and sometimes located in the right bundle branch, producing an idioventricular rhythm.

PARASYSTOLE

There were eighteen cases (0.03 per cent) in which several premature ventricular contractions had similar configuration but bore an inconstant relationship to the preceding normal beat, thereby establishing the diagnosis of ventricular parasystole. Numerous examples of fusion beats from the sinus node and ventricular foci were noted in this group. (These eighteen

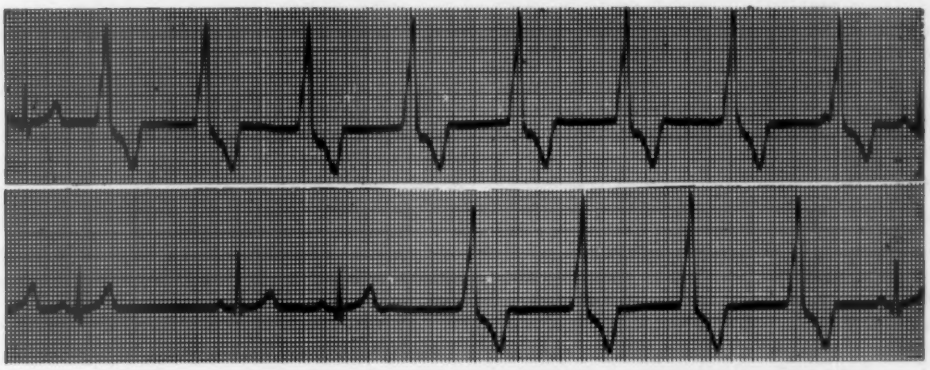


FIG. 12. Case 4. Continuous strip of lead II. Note that the majority of QRS complexes are ventricular in origin and mimic left bundle branch block. Recapture of the ventricles by the S-A node is seen in the first and last complexes of the upper strip and the last complex of the lower strip. A fusion beat of the two foci is seen in the second complex of the lower strip.

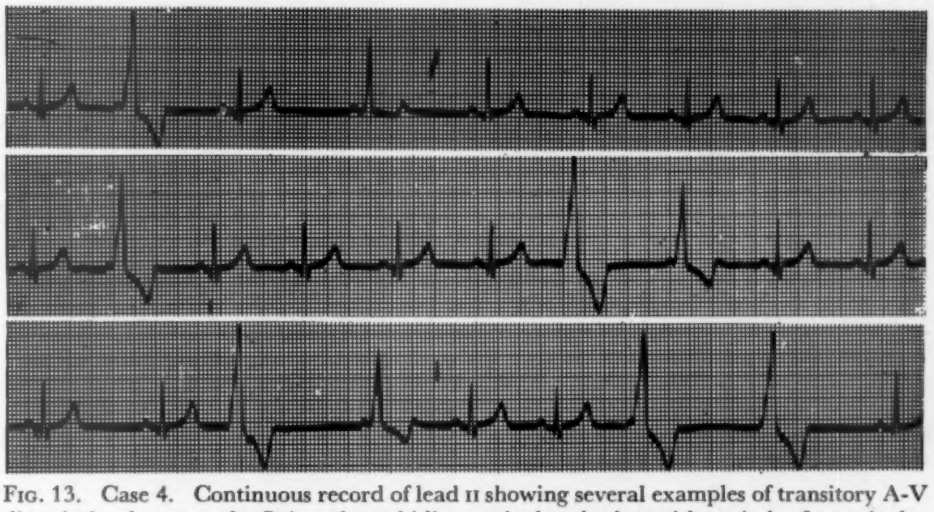


FIG. 13. Case 4. Continuous record of lead II showing several examples of transitory A-V dissociation between the S-A node and idioventricular rhythm with periods of ventricular capture by the S-A node intervening. Note the fusion beats in the fourth complex of the upper tracing and the third complex from the right in the middle tracing.

cases are not included in the 419 cases described in the section on isolated ventricular premature contractions.)

The average age of this group was 30.5 years with a range of nineteen to forty-one. The incidence figure for ventricular parasystole is quite small (0.03 per cent). It is entirely possible that many of the cases of ordinary premature ventricular contractions might have been diagnosed as parasystole if a longer electrocardiographic record had been obtained. A parasystolic focus which only occasionally breaks through its exit block and become manifest may be missed by the mass survey method employed in this study. The true incidence of ventricular parasystole in the asymptomatic population is undoubtedly higher than indicated by our figures, but it is believed that the incidence of relatively active parasystolic foci which become manifest at frequent intervals was accurately assessed.

Two of the eighteen subjects showed repetitive, successive ventricular contractions of parasystolic origin, so that the inherent rate of the focus could be calculated. It was approximately 150 in both of them. One demonstrated a parasystolic focus which appeared to arise from one of the bundle branches.[11] A long strip (lead II) from the second subject is shown in Figure 14. Several examples of two successive parasystolic beats at a high rate are visible. These two subjects were not considered good candidates to continue their flying career as it was thought that their parasystolic foci might at any time assume cardiac excitation and produce paroxysmal ventricular tachycar-

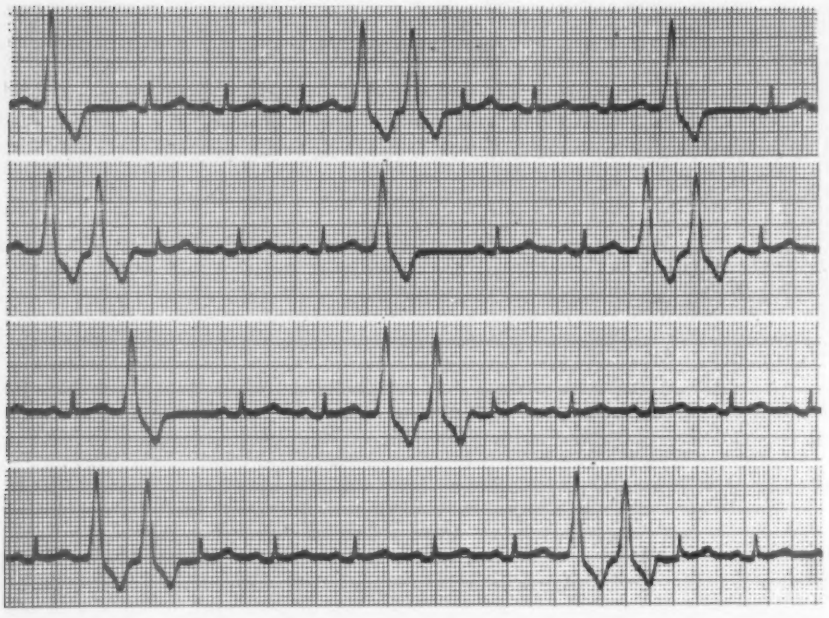


FIG. 14. Ventricular parasystole with numerous examples of two successive ectopic beats at a high rate.

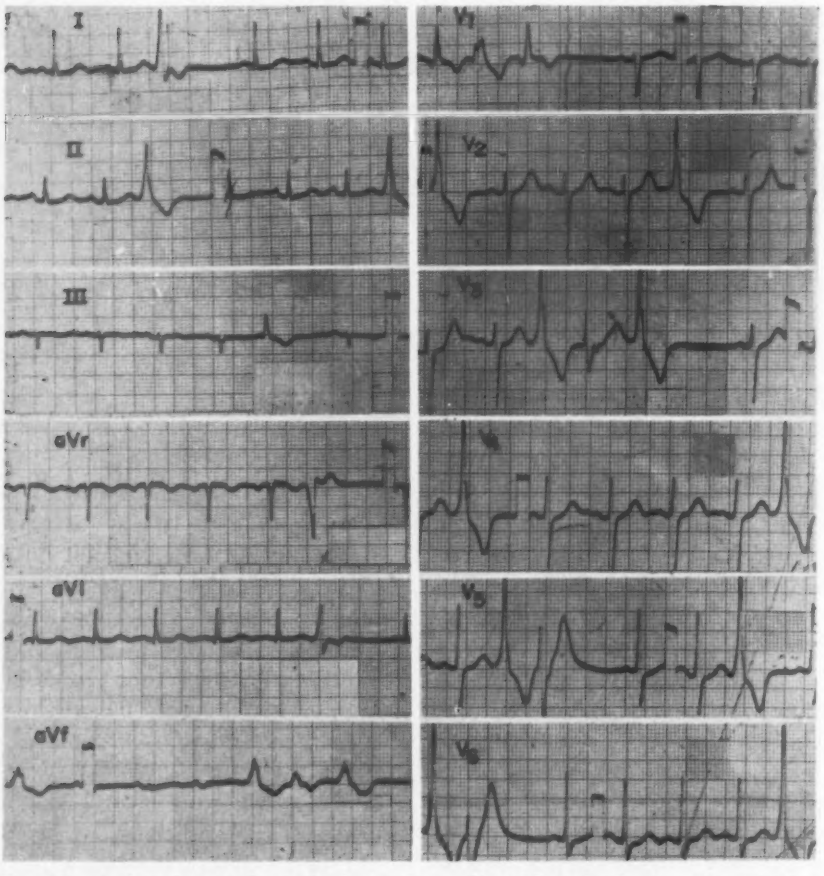


FIG. 15. A short burst of ventricular tachycardia. Note the frequent ventricular premature contractions throughout the tracing which occur three times consecutively in lead aVF. This fulfills the criteria for ventricular tachycardia.

dia with its attendant alterations of cardiovascular hemodynamics. This is particularly true during periods of sinus bradycardia or sinus arrest when a parasystolic focus may become free of the suppressive effect of the normal pacemaker. Stresses attendant to flying are known to induce cardio-inhibitory responses, thereby exaggerating the potential danger of an active parasystolic focus in an aviator.

VENTRICULAR TACHYCARDIA

The example of ventricular tachycardia was discovered in a subject who was otherwise asymptomatic and considered himself in good health. He was thirty-five years old. His routine electrocardioagram (Fig. 15) showed numerous examples of interpolated ventricular premature beats. However, there is one example of a short burst of ventricular tachycardia in lead aVF consisting of three consecutive ventricular complexes. Three consecutive ectopic venticular beats premature in onset occurring at a relatively fast rate (approximately 136 in this subject) meet the criteria for ventricular tachycardia.[5] The ectopic beats and the tachycardia are probably not parasystolic, as the isolated premature contractions are apparently fixed to the preceding normal complex and the short burst of tachycardia is not regular. No common denominator for the intervals between ventricular beats could be found.

SUMMARY

An electrocardiographic analysis of 67,375 healthy, asymptomatic men has been conducted and the incidence of various types of ventricular rhythms determined. All known forms of ventricular rhythm were detected except ventricular flutter and ventricular fibrillation.

Four hundred nineteen cases of premature ventricular contractions were noted (0.6 per cent), of which twenty-two were interpolated and one multifocal. Bigeminy, trigeminy and quadrigeminy were each noted in a few subjects.

There was a twofold increase in the rate of premature ventricular contractions per 1,000 subjects in the forty to forty-four year age group as compared to the younger age groups, and a threefold increase above forty-five years of age.

The average heart rate of subjects with numerous premature ventricular contractions was the same as that of subjects with rare premature beats, indicating that heart rate is not a significant determinant of the frequency of ectopic ventricular beats.

The ratio of premature ventricular contractions originating in the right ventricle (QRS pattern of left bundle branch block) to those from the left ventricle (QRS pattern of right bundle branch block) was 3 to 1. There was a fourfold increase in the rate per 1,000 of the former from the youngest to the oldest age group, but no increase in rate of the latter with age.

There were eighteen subjects with ventricular parasystole (0.03 per cent) and one with ventricular tachycardia.

Four subjects with idioventricular rhythm with A-V dissociation were presented. These demonstrate the passive assumption of control of cardiac excitation by a ventricular focus upon slowing or failure of the sinus node. This occurred in preference to either an atrial or nodal focus which in most subjects are active under such circumstances.

REFERENCES

1. AVERILL, K. H. and LAMB, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
2. SCHERF, D. and SCHOTT, A. Extrasystoles and Allied Arrhythmias, p. 453. London, 1953. William Heineman.
3. WHITE, P. D. and SPRAGUE, H. B. Electrocardiography of 10,000 patients at the Massachusetts General Hospital from 1914 to 1931. *Kasan M. J. (U.S.S.R.)*, p. 381, 1931.
4. WHITE, P. D. Heart Disease, 4th ed., p. 800. New York, 1951. The Macmillan Co.
5. KATZ, L. and PICK, A. Clinical Electrocardiography. Part I. The Arrhythmias, pp. 43, 290. Philadelphia, 1956. Lea & Febiger.
6. GRAYBIEL, A., MCFARLAND, R. A., GATES, D. C. and WEBSTER, F. A. Analysis of electrocardiograms obtained from 1000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
7. STEWART, C. B. and MANNING, G. W. Detailed analyses of the electrocardiograms of 500 R.C.A.F. aircrew. *Am. Heart J.*, 27: 502, 1944.
8. DAUWE, F. L'extrasystole clinique. *Bull. soc. belge cardiol.*, 5: 164, 1938.
9. AVERILL, K. H., FOSMOE, R. J. and LAMB, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. II. Supraventricular rhythms. *Am. J. Cardiol.*, 6: 84, 1960.
10. LAMB, L. E. and AVERILL, K. H. Less commonly recognized actions of atropine on cardiac rhythm. *Am. J. M. Sc.*, 237: 304, 1959.
11. LAMB, L. E., DERMKSIAN, G. and SARNOFF, C. A. Significant cardiac arrhythmias induced by common respiratory maneuvers. *Am. J. Cardiol.*, 2: 563, 1958.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

IV. Wolff-Parkinson-White Syndrome*

CAPT. KEITH H. AVERILL, MC, USAF, CAPT. ROBERT J. FOSMOE, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THE ELECTROCARDIOGRAPHIC entity of a short P-R interval and prolonged QRS duration has been known by different names. Originally called short P-R interval with bundle branch block[1] it has since been referred to as the Wolff-Parkinson-White syndrome, pre-excitation syndrome,[2] anomalous atrioventricular excitation[3] and accelerated nodal conduction.[4] Because the term WPW syndrome has been used for many years and its meaning is generally known this term will be used here.

Although numerous reports have been published on series of patients observed in hospitals and clinics, no large survey has been made of subjects with this entity found in an asymptomatic population. This report is of 109 new cases of the WPW syndrome, 106 of which were found by an electrocardiographic survey of 67,375 asymptomatic, healthy subjects.

Excellent case reports and reviews elucidating the clinical, electrocardiographic and anatomic features and the theories of the pathogenesis of this interesting conduction anomaly have been published since the first description by Wilson in 1915.[5–36]

MATERIAL AND METHODS

In the analysis of 67,375 electrocardiograms recorded either as a part of the physical evaluation for flying training or as a part of the annual physical examination of trained flying personnel, 106 cases of the WPW syndrome were discovered. In addition, three cases are included which were discovered prior to the electrocardiographic survey.

Sixty-seven of these subjects have been seen in consultation and a comprehensive cardiovascular evaluation carried out for each. Specialized electrocardiographic procedures utilizing a four-channel instrument included continuous tracings during rhythmic deep breathing, breath-holding, hyperventilation followed by breath-holding, carotid sinus massage, sitting, standing and following rapid intravenous injection of 1.2 mg. atropine sulfate. A double Master exercise test was performed in most instances. A quantitative vectorcardiographic analysis was also performed in each subject. The remaining forty-two subjects who were not evaluated in this laboratory had all been subjected to a thorough examination at the facility at which their initial electrocardiograms were recorded. Direct communication with the physicians who examined these subjects was carried out in most instances.

RESULTS

INCIDENCE

Only those subjects with an established rhythm of complexes with a short P-R interval and a prolonged QRS duration with a prominent delta wave were included. Records showing only a short P-R interval without aberration of the QRS complexes[37] were not included. The 106 cases of the WPW syndrome represented 0.16 per cent of the 67,375 subjects surveyed or a rate of 1.6 per 1,000.

Figure 1 shows the *age distribution* for the subjects with the WPW syndrome compared to the age distribution for the entire survey. The curves are nearly identical. Table 1 gives the rate per thousand for the WPW syndrome in the various age groups. No significant concentration of these cases was found in either the younger or the older age groups. The incidence of the WPW syndrome has been reported in other series representing various

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

TABLE I
Incidence of WPW Syndrome per Thousand Subjects by Five-Year Age Groups

Age (yr.)	Rate per Thousand
Under 20	3.2
20–24	1.8
25–29	1.6
30–34	1.8
35–39	1.3
40–44	1.0
45 and over	2.9

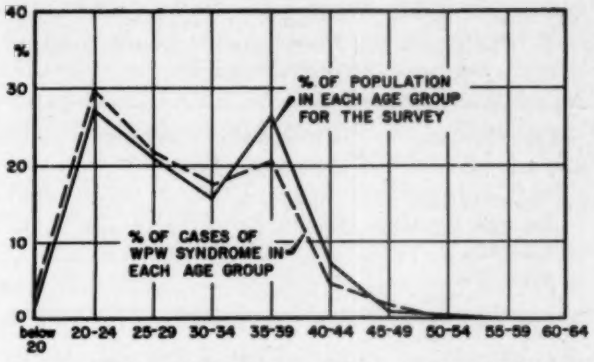


FIG. 1. The age distribution of subjects with WPW syndrome is compared to the age distribution for the total population surveyed.

groups—some in hospitalized and some in non-hospitalized patients.[10,22,38–43] The incidence of the WPW syndrome in the larger series is tabulated in Table II. Between one and two cases per thousand were the figures most commonly recorded.

Such an even distribution among the various age groups is consistent with the concept that the WPW syndrome is, indeed, of congenital origin. Recent reports of the WPW syndrome in newborn infants and children[7,8,45–50,69] and in members of the same family[2,51–53] point up the importance of congenital and familial factors in this condition.

The *sex incidence* in the WPW syndrome is usually stated to be predominantly male. The exact incidence of the WPW syndrome in the asymptomatic female population has not been established.

ASSOCIATED HEART DISEASE

None of the 109 subjects examined showed any indication of organic heart disease. Sixty-seven were evaluated in this laboratory and are the basis for the following comments:

Five had systolic murmurs which were considered insignificant. None had had diphtheria, rheumatic fever or myocarditis. Three had had scarlet fever, one of whom also had recurrent nose bleeds up to the age of twenty-two. There was no indication of rheumatic valvulitis in this subject. One patient had experienced one episode of vague pain in the chest which was not considered to be of cardiac origin. One subject had infectious mononucleosis at the age of sixteen. One subject had experienced early rheumatoid arthritis of the hands; one had a labile blood pressure and was classified as a vascular hyperreactor; one subject had diagnosis of pulmonary coccidioidomycosis made at the age of twenty-five, for which he was hospitalized for six weeks; another had had hepatitis; and one had passed a urinary calculus. Another had a history of recurrent infection of the upper respiratory tract of unknown etiology. No significant abnormalities were noted in the roentgenograms of the chest in any of these subjects. The total cholesterol (Bloor method) and phospholipid values (Fiske-Subbarow technic) are

TABLE II
Incidence of the WPW Syndrome in Previous Series

Authors	Rate per Thousand	Type of Study
Wolferth and Wood[10] (1933)	1	
Hunter, Papp and Parkinson[22] (1940)	0.16	19,000 electrocardiograms from Cardiac Department of London Hospital
	0.57	14,000 electrocardiograms from consulting practice
Kaplan and Cohn[38] (1944)	1.2	1,672 electrocardiograms from Army station hospital
Graybiel et al.[41] (1944)	2	1,000 healthy naval aviators
Littman and Tarnover[39] (1946)	2.4	3600 electrocardiograms from hospitalized subjects
Reed, Langley and Utz[40] (1947)	1.2	6,900 electrocardiograms from a U. S. Naval Hospital
Manning[42] (1954)	2	5,000 healthy aircrew members
Hejtmancik and Herrmann[43] (1957)	1.4	55,000 electrocardiograms from University of Texas School of Medicine

TABLE III
Serum Cholesterol and Phospholipid Levels in Subjects with the WPW Syndrome

Mg. Per Cent	Cholesterol	Phospholipids
Less than 200	12	3
200–249	23	22
250–299	18	30
300 and over	10	6

given in Table III. None of the subjects knew of any instances of the WPW syndrome in their immediate families. There was no increased incidence of degenerative heart disease in their families. Five gave a definite history of some member of their immediate family having died of degenerative heart disease. One subject had a daughter with a ventricular septal defect.

The singular absence of organic heart disease in this group of subjects was not unexpected since they represent a select group who had undergone rigid physical evaluations before entering the Air Force aviation program.

Congenital Heart Disease: It is generally considered that the appearance of significant organic heart disease is usually coincidental in patients with the WPW syndrome. The association of the WPW syndrome with congenital heart disease has been noted in several reports.[43,44,55] With the probable exception of Ebstein's anomaly, the association of other congenital heart defects with the WPW syndrome may well be coincidental.

Acquired Heart Disease: In considering the incidence of all types of heart disease in the WPW syndrome in the larger series that have been reported it must be remembered that most were hospitalized patients undergoing evaluation for various symptoms. Among fifty-two patients Wolff and White[54] found ten (20 per cent) who had some disease of the heart other than the abnormal electrocardiogram or paroxysmal tachycardia. Willius and Carryer[56] found cardiac disease in 29.2 per cent of sixty-five patients. Among nineteen patients in this group, five had healed rheumatic valvular disease, four had coronary artery disease with angina pectoris, nine had hypertensive cardiovascular disease and one had an adenomatous goiter with hyperthyroidism and congestive failure. Hejtmancik and Herrmann[43] found that thirty-two (40 per cent) of their eighty patients had some type of organic heart disease. They state, however, that most of these patients

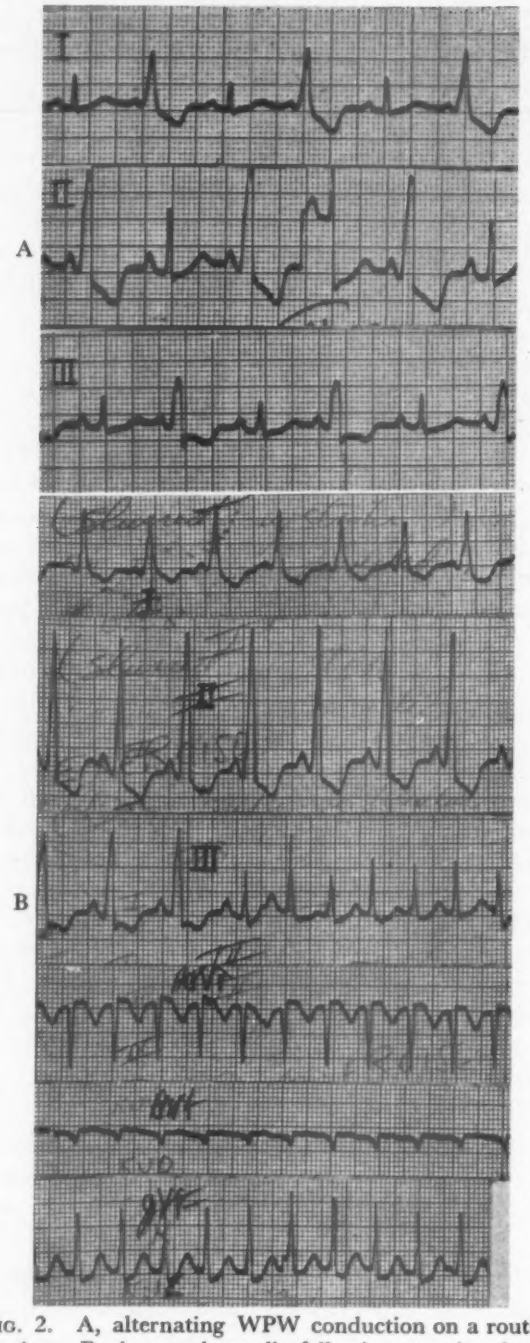


FIG. 2. A, alternating WPW conduction on a routine tracing. B, sinus tachycardia following exercise changing to paroxysmal atrial tachycardia in leads III, aVR and aVF.

with heart disease were over forty years of age and that nineteen of them had coronary artery disease. Other than Ebstein's abnormality, no direct correlation has been made between any type of organic heart disease and the syndrome under discussion. There is no conclusive evidence that the WPW syndrome ever develops as a result of acquired heart disease. The vast majority with this syndrome appear

to be asymptomatic and lead normal lives. Chance alone could account for those few patients who have been reported who have demonstrated the WPW syndrome in addition to such findings as rheumatic heart disease, arteriosclerotic heart disease or congenital heart disease.

The most common type of heart disease in patients with the WPW syndrome is that of iatrogenically produced cardiac neurosis. Usually this occurs when the electrocardiogram has been misinterpreted as perhaps showing left bundle branch block or evidence of coronary artery disease or when the significance of paroxysmal rapid heart action has not been thoroughly explained.

PAROXYSMAL TACHYCARDIA

One of the distinguishing characteristics of patients with the WPW syndrome is the high incidence of paroxysmal tachycardia. It was expected that its incidence in this group of subjects would be small, inasmuch as persons who have recurrent episodes or unexplained single episodes of paroxysmal tachycardia are usually not retained for flying duties. It was found that eight (12 per cent) of the sixty-seven subjects who were evaluated in this laboratory had a history consistent with paroxysmal rapid heart action. Three of these had electrocardiographic documentation of at least one of the episodes of tachycardia; all were supraventricular in nature with normal QRS duration.

Of particular interest was a twenty-seven year old pilot with a history of two episodes of paroxysmal tachycardia, both of which caused only mild shortness of breath and subsided spontaneously within an hour. A routine tracing taken prior to an exercise tolerance test showed intermittent anomalous atrioventricular excitation. Immediately after exercise the heart rate increased to 120 per minute and WPW conduction was persistent until interrupted by a normally conducted beat in lead III which precipitated the onset of a paroxysmal supraventricular tachycardia (Fig. 2 A and B).

One subject had experienced only one episode of tachycardia, apparently precipitated by an episode of coughing. This caused mild generalized weakness and was aborted only after intravenous administration of lanatoside C. Two subjects had experienced multiple episodes, one from early childhood and the other beginning at the age of twenty years. Both had only a sensation of palpitation during the short episodes. One subject had experienced five to six episodes associated with a sensation of palpitation with the onset at age thirty-three. One had two brief suggestive episodes, both associated with only slight shortness of breath and awareness of a fast heart rate. Two subjects, aged twenty-seven and thirty-five, had experienced several episodes of tachycardia manifested by palpitation and breathlessness. This resulted in near syncope in one and in two episodes of unconsciousness in the other. Of these eight subjects, five had experienced the onset of tachycardial episodes prior to the age of thirty and four after the age of thirty.

The incidence of paroxysmal tachycardia in the WPW syndrome has been found by others to range from 40 to 80 per cent.[10,22,43,54,56] The true incidence of paroxysmal tachycardia is difficult to determine. These high percentages were reported, for the most part, from series in which the patients had sought medical care because of symptoms. The low incidence in the present study also does not represent the true incidence of paroxysmal tachycardia in the WPW syndrome since people entering flying training are carefully screened for a history of paroxysmal tachycardia and those who have had significant symptoms would either not have applied for pilot training or would have been rejected. This would certainly alter the incidence since it appears that for the majority of patients with the WPW syndrome paroxysmal tachycardia, if it develops, will appear before the age of thirty. For example, 126 cases from the literature were reviewed in which the diagnosis of paroxysmal tachycardia had been made and the age of onset given. In 76 per cent of these subjects, time of the onset of paroxysmal tachycardia was below the age of thirty, whereas only 24 per cent of them had onset at age thirty or above. The deleterious effects of paroxysmal tachycardia is greater in infants[62] and in older people.

It became apparent after a number of cases of paroxysmal tachycardia in the WPW syndrome had been reported that the QRS complexes were not always of normal configuration during the episode of tachycardia.[8,10,24,43,48,54,56–60] This is particularly true in those whose paroxysmal tachycardia is due to either atrial fibrillation or atrial flutter, rather than paroxysmal atrial tachycardia. In many instances this had earlier been misinterpreted as being an irregular ventricular tachycardia rather than atrial flutter

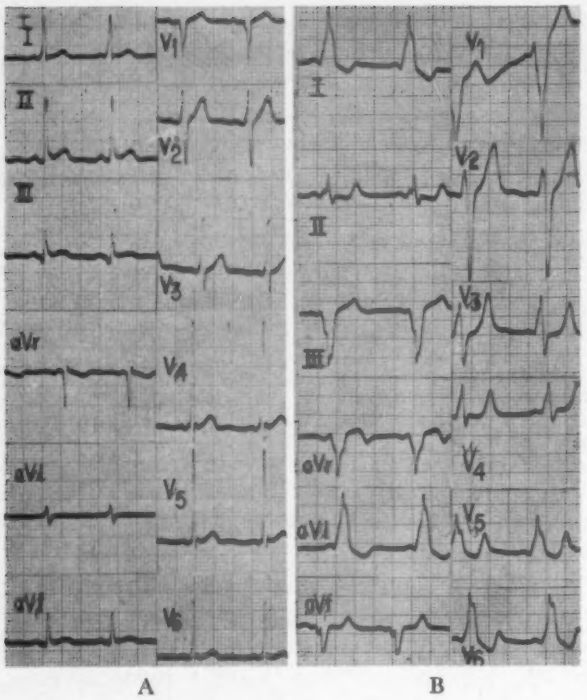


FIG. 3. A, minimal evidence of pre-excitation in lead I and the V leads with relatively normal S-T segment and T waves. B, markedly aberrant ventricular excitation with secondary S-T segment and T wave changes.

or fibrillation with QRS aberration.[29,61] In some cases it may be quite difficult to distinguish between the two arrhythmias. The necessity for distinguishing true ventricular tachycardia from supraventricular tachycardia with aberrant conduction is important from standpoints of prognosis and treatment.

ELECTROCARDIOGRAPHIC CHARACTERISTICS

The electrocardiographic diagnosis of the WPW syndrome is not difficult. For the most part, the electrocardiograms of patients with this syndrome have characteristic features. The usually described characteristic of the electrocardiogram is the short P-R interval followed by a prolonged QRS complex in which the early portion is slurred. The initial slurring of the QRS complex, designated as the delta wave, is of low amplitude and of varying duration. The electrical forces creating the delta wave may be represented vectorially as a spatial force. The delta wave in some tracings may be represented by a small deflection which in some leads may return to the baseline prior to the recording of the rest of the QRS complex. This has been designated the X wave by Öhnell.[2] Wolferth and Wood[10] stress that the P-J interval decreases in duration and that the slurring always involves the initial portion of the QRS complex. However, the P-J interval may be prolonged in WPW conduction in those rare cases with delay in conduction across the A-V junction. This can be identified when prolongation of the P-R interval is apparent in the presence of intermittent normal ventricular excitation.

Refinements of the aforementioned characteristics have been developed over the years. It is now apparent that the QRS duration does not necessarily have to be abnormally prolonged and may be below 0.12 second. However, in order for the diagnosis to be made, the QRS complex must still show the initial slurring which makes it abnormal in configuration, although not necessarily abnormal in duration. The duration and configuration of the QRS complex would seem to be determined by the extent of anomalous excitation. In some instances the QRS configuration is abnormal only in that small delta waves are present in the initial portion; in others the QRS duration is noticeably prolonged and the QRS configuration is markedly abnormal. In the former it appears that only a small portion of the heart is excited in an anomalous fashion and that aside from the initial slurring the remainder of the QRS complex is produced by normal intraventricular conduction while in the latter, intraventricular conduction is entirely abnormal, perhaps representing almost complete anomalous excitation. Figure 3A shows an electrocardiogram from a person in whom the WPW syndrome is present and is characterized by a short P-R interval with an essentially normal QRS complex except for the initial early slurring. There are no significant S-T segment or T wave changes. The routine electrocardiogram from another subject (Fig. 3B) demonstrates the marked change in intraventricular conduction with secondary S-T segment and T wave changes which may be seen in the WPW syndrome.

P-R and QRS Intervals: Sixty-six subjects had simultaneously recorded leads while showing anomalous excitation. The determination of the P-R intervals and QRS durations without simultaneous leads is often inaccurate, as pointed out by White.[63] Table IV gives the results obtained for the P-R interval, QRS duration and P-J interval in these sixty-six subjects. Forty-three (65 per cent) had a P-R interval of 0.10 second or greater. The QRS duration was 0.10 second or greater in all these subjects and 0.12 second or greater in the majority.

TABLE IV

Electrocardiographic Values Using Simultaneous Leads in Sixty-Six Subjects with WPW Conduction

Second	P-R Interval	QRS Duration	P-J Interval
0.07	2	..	..
0.08	5	..	..
0.09	16	..	..
0.10	25	6	..
0.11	8	4	..
0.12	10	27	..
0.13	..	15	..
0.14	..	11	..
0.15	..	1	..
0.16	..	1	..
0.17	..	1	..
0.18	..	..	..
0.19	..	..	1
0.20	..	..	8
0.21	..	..	14
0.22	..	..	14
0.23	..	..	5
0.24	..	..	19
0.25	..	..	3
0.26	..	..	1
0.27	..	..	..
0.28	..	..	1

The P-J interval was greater than 0.24 second in only five instances. When simultaneous leads were used, only seven of these subjects had a P-R interval of 0.08 second or less. The length of the P-R interval depends on its duration when normal conduction is present and the amount of pre-excitation when the WPW syndrome is present. Thus, no fixed limit for the P-R interval applies to all. As an example, one patient in this series had a normal P-R interval of 0.20 second and a QRS duration of 0.12 second, while in another variant of WPW conduction, the P-R interval was 0.11 second and the QRS duration was 0.17 second.[76] An intermittent normal record is necessary to demonstrate this point.

QRS Axis: The mean QRS axis in the frontal plane was determined in 108 subjects (Table v). There is obviously a wide variation. The orientation of the delta wave axis in the frontal plane was also determined (Table v). The range is also wide and not too dissimilar from that of the QRS axis, although there were more subjects with a vertically oriented vector. Only 22 per cent had more than a 30 degree difference between the axis for the delta wave and the QRS axis in the frontal plane. This may mean that the spatial direction of the initial delta forces determines to a great extent the pathway for subsequent ventricular excitation and thus the spatial orientation of the mean QRS vector.

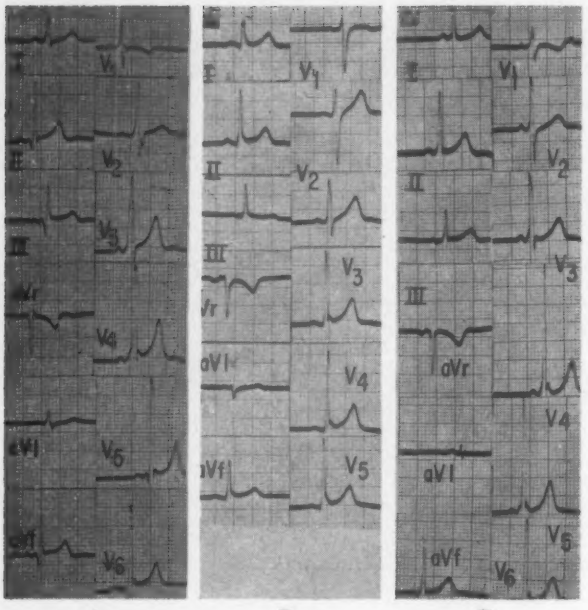
TABLE V

Mean QRS and Delta Axes in Frontal Plane of 109 Subjects with WPW Conduction

Axis (degrees)	QRS (no.)	Delta (no.)
− 60	1	2
− 45	6	3
− 30	5	16
− 15	10	8
0	15	15
+ 15	9	5
+ 30	6	11
+ 45	9	9
+ 60	21	14
+ 75	13	4
+ 90	9	7
+105	3	5
+120	1	10

In the transverse plane initial forces are usually directed anteriorly and are of sufficient amplitude to alter the usual R/S ratios in the precordial leads. Of the 109 subjects, 107 had an upright or isoelectric delta wave in lead V_2. Of these 107, eighty-seven (81 per cent) had an R wave equal to and usually greater than the S wave in lead V_2. This abnormality of the R/S ratio in the precordial leads is a distinctive characteristic of the majority of tracings demonstrating the WPW syndrome. Only two subjects were found to have an inverted delta wave in leads V_1 and V_2, representing a posteriorly directed initial force. In both instances, prominent QS deflections were present in leads V_1 and V_2.

Classification of WPW Syndrome: An electrocardiographic classification of the WPW syndrome has been proposed by several investigators, based on the direction of the delta wave and QRS complexes in various leads.[2,31,64] Rather than making an empirical classification based on minute changes in configuration or vector analysis in only the frontal or transverse plane, it would seem preferable to describe the electrical events vectorially in each case. In this way a complete description of the electrocardiogram can be obtained in a succinct manner without resorting to artificial classifications. All that is necessary is to describe the mean axis of the delta wave in the frontal plane and its



A B C

FIG. 4. A, the question of pre-excitation in the limb leads is clarified by using the V leads, in which the delta wave is more distinct. B, an electrocardiogram with a short P-R interval and normal QRS. C, a repeat electrocardiogram in the same subject demonstrates pre-excitation.

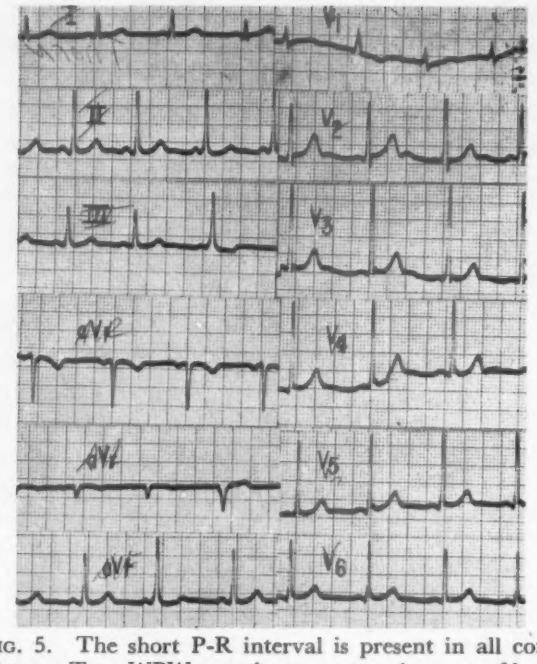


FIG. 5. The short P-R interval is present in all complexes. True WPW complexes are seen in parts of leads II, III and aVF and elsewhere in the record.

transition zone in the precordial leads in addition to the vector analysis of the remaining QRS complex.

In most examples of the WPW syndrome a prominent delta wave will be present in many leads associated with a short P-R interval. Occasionally the delta wave in the standard limb leads will be small, creating a distinct deflection which returns almost to the baseline. Some confusion may arise in differentiating this from a notched P wave. The appearance of the precordial leads, however, readily makes this differentiation (Fig. 4A).

Short P-R Interval and Normal QRS Complex: Confusion exists as to whether or not those electrocardiograms with a very short P-R interval and a normal QRS complex represent some variation of the WPW syndrome. The answer is not definitely known, although Lown, Ganong and Levine[37] believe the syndrome of a short P-R interval and a normal QRS complex is distinctly separate from that under discussion. However, they have made the interesting observation that these subjects also tend to be more susceptible to paroxysmal rapid heart action than those who have a normal P-R interval. This series has not included subjects in whom the QRS complex was completely normal, although it does appear that some may well represent examples of a variation in the WPW syndrome.

An example of this problem is seen in Figure 4B, which shows a short P-R interval without a definite isoelectric period between the end of the P wave and the onset of the QRS complex, but no distinct delta wave. A repeat electrocardiogram taken eight months later (Fig. 4C) demonstrates shortening of the P-R interval and a delta wave most distinct in the precordial leads. The electrocardiogram from another subject with intermittent WPW demonstrates the problem (Fig. 5). During the period of normal conduction the P-R interval is short without an isoelectric interval between the P wave and the onset of the QRS complex. The electrocardiogram of a third subject (Fig. 6) shows a short P-R interval with a normal QRS complex. This subject was thoroughly studied and numerous tracings recorded. No definite diagnostic initial slurring of the QRS complex was ever noted. Such electrocardiograms are not infrequently seen and present some difficulty since some leads appear to have small delta waves which are not distinctive enough to permit a definite diagnosis.

Spatial Orientation of QRS Axis: The spatial orientation of the delta wave and the spatial orientation of the QRS axis have a wide range.

The electrocardiogram from a subject with a delta wave axis of +120 degrees in the frontal plane is seen in Figure 7A. The striking Q wave in leads I and aVL is produced by the electrical forces

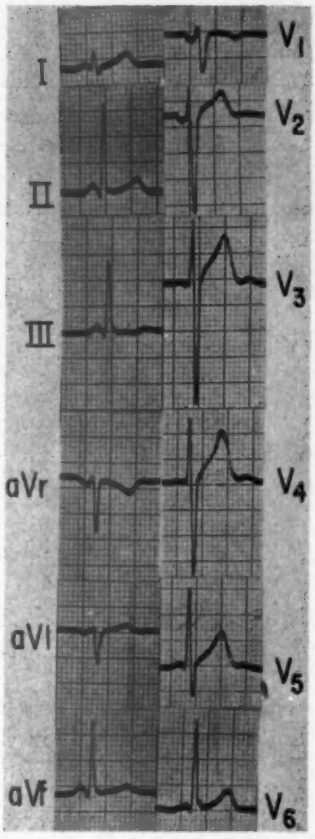
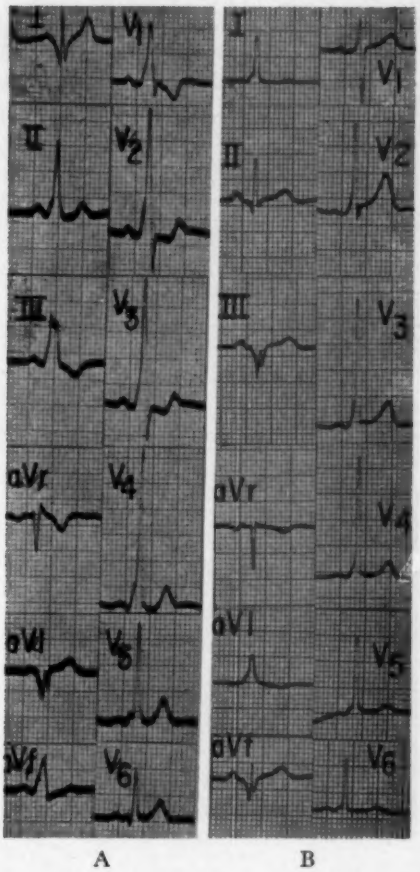


FIG. 6. An example of the short P-R interval without evidence of pre-excitation.



A B

FIG. 7. A, the pre-excitation vector results in Q waves in leads I and aVL. B, the pre-excitation vector results in Q waves in leads III and aVF.

responsible for the delta wave seen in the precordial leads. This is associated with the large R waves in leads V_1 and V_2, one of the most common electrocardiographic findings in the WPW syndrome. An electrocardiogram from another subject demonstrates a delta wave axis in the frontal plane of −60 degrees (Fig. 7B). This creates a large QS deflection in lead III. Such large Q waves may be mistaken for evidence of myocardial infarction of the inferior wall when the WPW syndrome is not recognized. A large R wave in lead V_2 is again apparent.

ELECTROCARDIOGRAPHIC VARIATIONS

Intermittent WPW Conduction: One feature of the WPW syndrome is its intermittent nature in many subjects. The electrocardiogram may show abnormal complexes on one record and normal complexes on the next. Some subjects change from one to the other easily. Others change only after many maneuvers have been attempted. On some occasions normal QRS complexes and WPW complexes may alternate. Even though a previous normal electrocardiogram may have been recorded, a subject may resist conversion when evaluated during aberrant conduction despite all attempts to return ventricular excitation to normal. Others may show clear-cut electrocardiographic evidence of a WPW syndrome and then fail to show these changes over a long period of time despite numerous electrocardiographic tracings. Of the sixty-seven subjects who were evaluated thoroughly, thirty (44 per cent) showed normal QRS complexes at one time, either spontaneously or induced by various maneuvers. Electrocardiographic values before and after normalization are given in Table VI. At times it is difficult to determine whether complete or only partial normalization has occurred. The latter has been referred to as pseudonormalization and described as the *concertina effect* by Öhnell.[2] Changes in the configuration of the WPW complex are very common with maneuvers which increase or decrease vagal tone. Only those records in which it was considered that delta waves were no longer present in any of the leads are included as being normal.

Effect of Atropine: Administration of atropine has been commonly used to produce normal conduction in cases of the WPW syndrome.

TABLE VI
Electrocardiographic Values in Subjects During Normal and WPW Conduction

Case No.	During WPW Conduction					During Normal Conduction				
	P-R Interval	QRS Interval	P-J Interval	QRS Axis	T Axis	P-R Interval	QRS Interval	P-J Interval	QRS Axis	T Axis
1	0.12	0.14	0.26	+15	+90	...	0.08	...	...	...
3	0.09	0.12	0.21	+60	Undetermined	0.12	0.09	0.21	+60	+60
4	0.10	0.14	0.24	+90	+ 75	0.12	0.08	0.20	...	...
7	0.10	0.13	0.23	−30	+120	0.15	0.08	0.23	+90	−45
14	0.09	0.12	0.21	−15	+ 75	0.14	0.08	0.22	+90	−45
17	0.10	0.15	0.25	+45	Undetermined	0.18	0.09	0.27	+90	+75
18	0.11	0.13	0.24	+15	Undetermined	0.18	0.09	0.27	+90	+30
21	0.12	0.12	0.24	+45	+ 60	0.16	0.08	0.24	+75	+60
22	0.10	0.12	0.22	−30	+105	0.12	0.08	0.20	+30	−30
26	0.10	0.14	0.24	−30	+ 30	...	0.08	...	+30	−30
31	0.12	0.12	0.24	+15	+ 45	...	0.09	...	+75	−15
33	0.10	0.14	0.24	+60	+ 30	...	0.08	...	+60	+60
34	0.08	0.13	0.21	0	+ 60	...	0.07†	...	...	...
37	0.10	0.14	0.24	+90	+ 75	...	0.10	...	+75	+75
39	0.10	0.14	0.24	+75	+ 30	0.16	0.08	0.24	+75	+60
42	0.07	0.13	0.20	−45	0	...	0.10	...	−15	−45
44	0.09	0.13	0.22	0	+ 30	...	0.08	...	...	...
48	0.09	0.12	0.21	+90	+ 45	0.14	0.08	0.22	+60	+60
49	0.09	0.14	0.23	0	+ 75	0.18	0.08	0.26	+60	+45
51	0.10	0.13	0.23	−30	+ 75	0.16	0.09	0.25	+75	−45
53	0.12	0.12	0.24	0	+ 75	0.15	0.07	0.22	...	...
55	0.11	0.13	0.24	+30	+ 60	0.17	0.09	0.26	...	...
75	0.09	0.09	0.18	+75	+ 75	0.12	0.08	0.20	+75	+75
61	0.10	0.10	0.20	+60	+ 60	0.15	0.09	0.24	+75	+75
104	0.08	0.13	0.21	+60	+ 60	0.16	0.08	0.24	+60	+45
19*	0.11	0.17	0.28	+30	+ 45	0.20	0.10	0.30	+60	+60
	0.15	0.12	0.27	0	+105	...	...	...	...	...
63	0.10	0.12	0.22	+60	+ 60	0.14	0.08	0.22	+75	+45
6	0.10	0.12	0.22	+60	+ 60	0.16	0.07	0.23	+45	+45
66	0.10	0.12	0.22	+60	+ 60	...	0.07	...	...	...

* Two WPW variations.
† With paroxysmal atrial tachycardia.

The effects of atropine have been reviewed by numerous authors.[2,3,5,9,10,21,22,39,54,57,65–68,70] Normal conduction will not develop in all subjects after administration of atropine. The prevailing theory is that although vagal influences are not strictly responsible for the WPW syndrome they do, however, have some control over the amount of muscle excited anomalously. It has been stated that with increased vagal tone more impulses are carried over the accessory pathways and fewer impulses over the normal conduction system, while with decreased vagal tone more impulses are carried over the normal conducting system and fewer over the accessory pathways. The influence of vagal tone controlling the extent of impulses passing over the accessory pathway is responsible for the "concertina" effect.

In the present study fifty-six subjects with WPW conduction were given atropine sulfate (1.2 mg.) by rapid intravenous injection. Continuous electrocardiograms were obtained from the moment of injection until two minutes following the injection and then every minute for the next ten minutes. What appeared to be completely normal QRS complexes developed in eighteen subjects (30 per cent). This is a higher percentage than is usually reported and may well represent the advantage of giving atropine intravenously rather than subcutaneously or orally.

Of interest is the manner in which the normal QRS complexes were produced in the majority of these subjects. Normal QRS complexes were seen mainly when A-V dissociation with interference occurred. This was noted in thir-

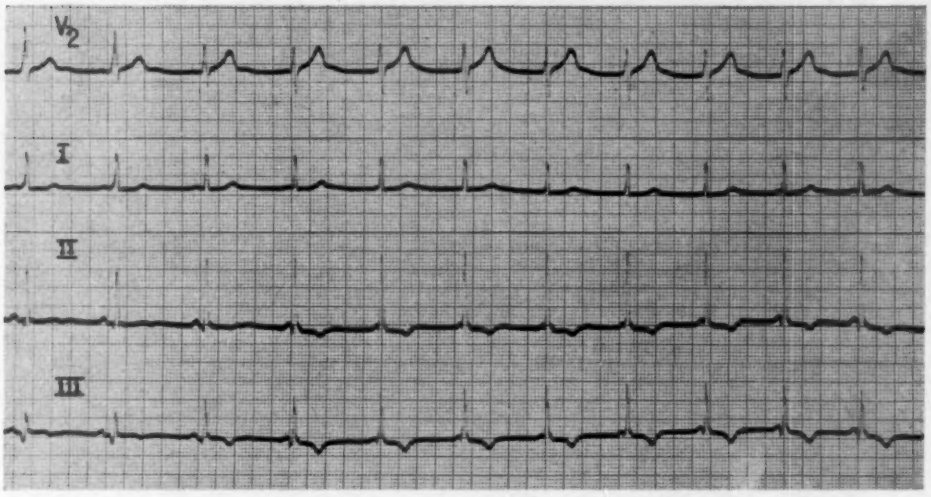


FIG. 8. Normalization of WPW conduction and A-V dissociation after administration of atropine.

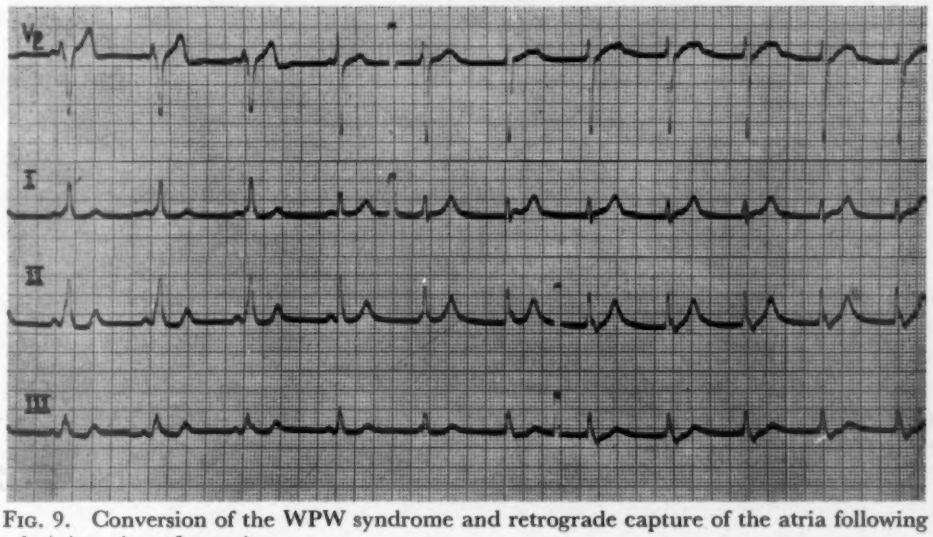


FIG. 9. Conversion of the WPW syndrome and retrograde capture of the atria following administration of atropine.

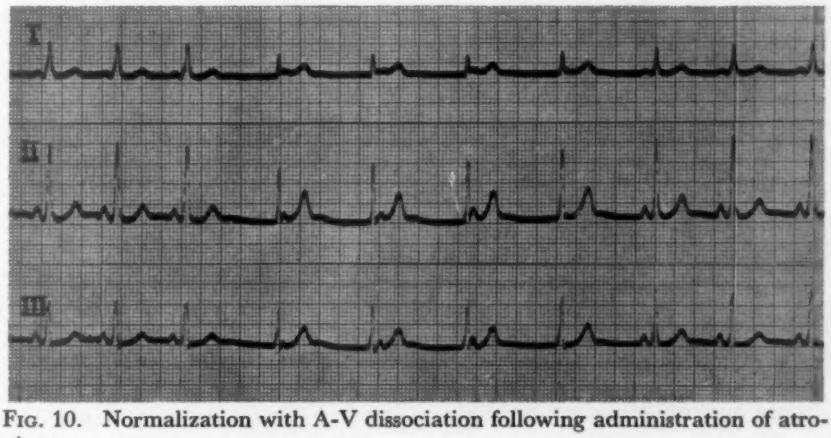


FIG. 10. Normalization with A-V dissociation following administration of atropine.

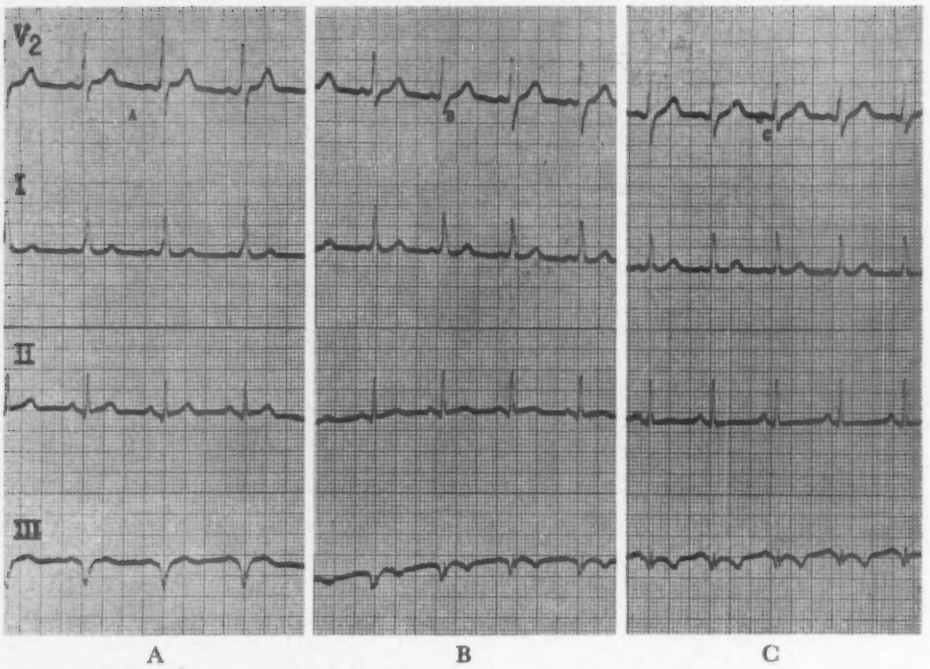


FIG. 11. Pseudonormalization of WPW conduction (A) before administration of atropine, (B) twenty seconds after administration of atropine and (C) one minute after administration of atropine.

teen of the eighteen subjects whose electrocardiograms became normal following administration of atropine. In this type of A-V dissociation the atria continue to be excited by the S-A node, but the ventricles are under control of the A-V node. In all instances in which A-V dissociation occurred after administration of atropine, QRS complexes of normal duration were seen. The phenomenon of A-V dissociation as an early manifestation of atropine activity has recently been reviewed.[70] When this occurs in patients with the WPW syndrome the QRS complexes are invariably of normal duration, and we are not aware of any instance in which A-V nodal excitation of the ventricles occurring after administration of atropine has failed to produce normal-appearing QRS complexes except when other coincidental conduction disturbances were present. Only two instances were seen in which administration of atropine without other associated maneuvers produced what appeared to be complete normalization without A-V dissociation. Three instances were seen in which normal complexes appeared after administration of atropine but in these, other maneuvers such as breath-holding and standing, were also necessary to produce normalization. It appears that atropine is most effective in producing normal-appearing QRS complexes when administered intravenously with continuous electrocardiographic recordings during the first two minutes after the injection. In this manner the short period of A-V dissociation is most likely to be found.

In Figure 8, leads V_2, I, II and III were recorded simultaneously shortly after intravenous administration of atropine sulfate. A prominent delta wave is seen in the first complexes of leads I and V_2. In leads II and III the delta wave is represented by the so-called X wave. A-V dissociation then occurs with the P wave gradually moving into the QRS complex and a definite change in ventricular conduction occurs with normalization of the QRS complexes. Toward the end of the strip the P waves move out of the QRS complex. T wave changes occur in leads II and III following A-V dissociation. After normalization T wave changes are a frequent occurrence in the WPW syndrome, both after the administration of drugs and following spontaneous normalization.

Figure 9 shows simultaneous leads recorded in another subject. When A-V dissociation occurred, a change in the QRS configuration appeared in the fourth QRS complex. The atria appeared to be stimulated by the S-A node during the fourth, fifth and sixth cycles, then atrial capture by the A-V node occurred, causing prominent inverted P waves following the QRS complex in the last five beats. The QRS complexes, however, were of normal duration. Here, again, as the A-V node assumed control of the ventricles, anomalous ventricular excitation seemed to disappear with definite normaliza-

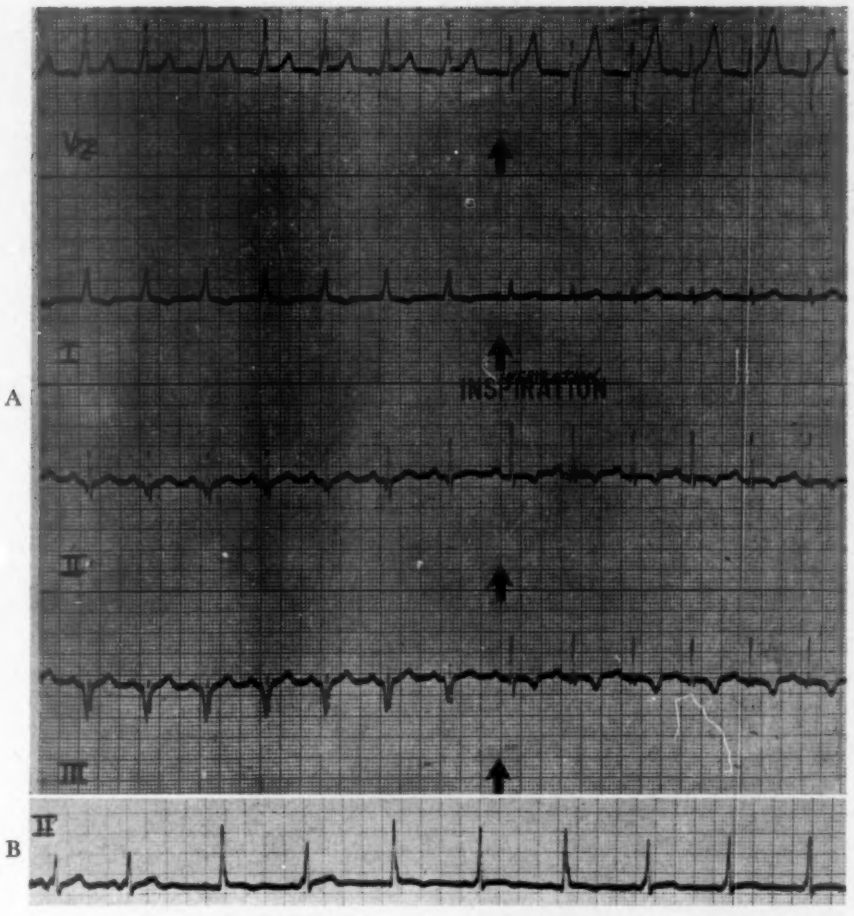


FIG. 12. Effects of breath-holding. A, conversion of WPW conduction to normal at the height of inspiration. The leads are recorded simultaneously. B, intermittent WPW conduction induced by breath-holding. The third, fifth and seventh beats appear normal. Increased abnormality of T waves associated with this change is noted.

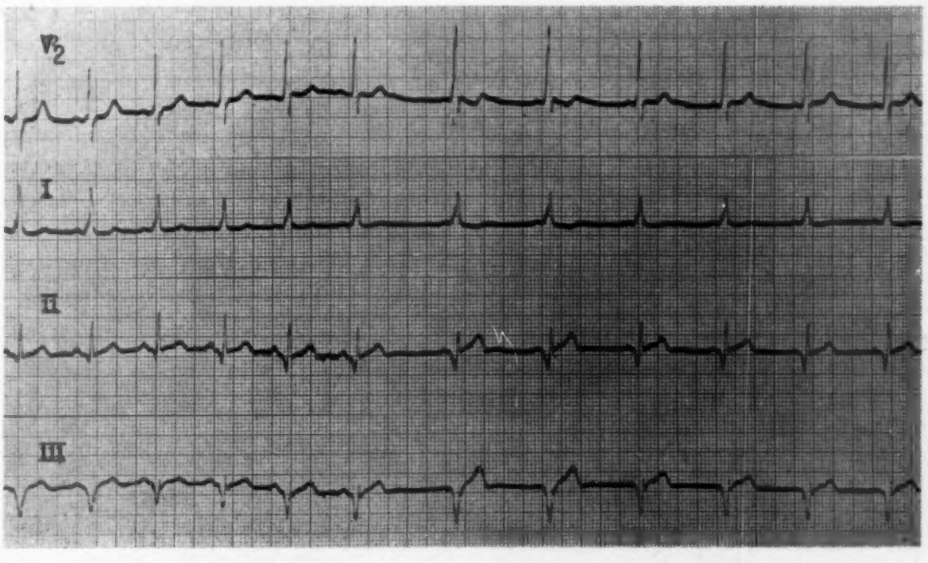


FIG. 13. At the height of inspiration, breath-holding decreases the cardiac rate and a striking change in QRS configuration occurs.

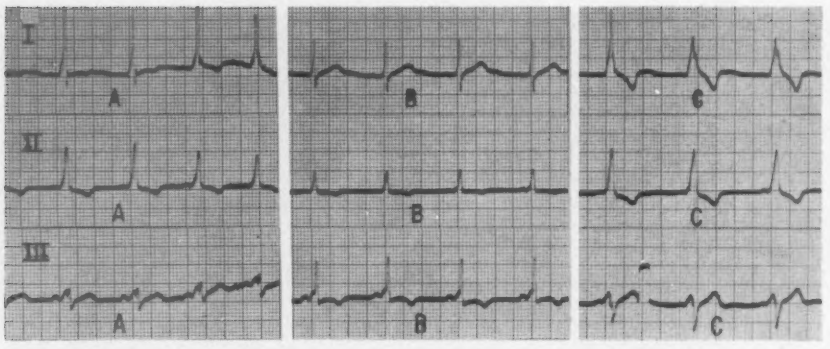


FIG. 14. Effect of breath-holding and deep expiration. A, WPW conduction in the resting record. B, during breath-holding a change in the QRS complex is noted. C, on exhaling further QRS changes occur.

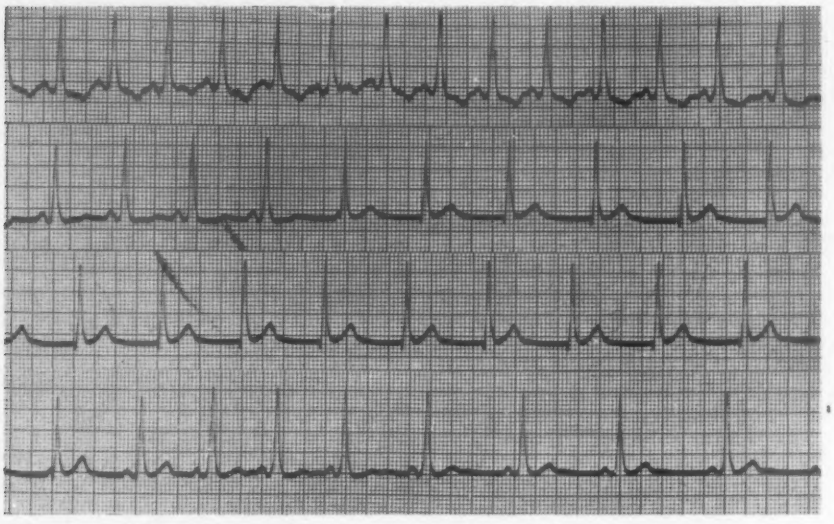


FIG. 15. Effect of hyperventilation and breath-holding. In the first strip of a continuous lead II tracing WPW conduction is present with a short P-R interval and a definite delta wave. Hyperventilation to the point of symptoms was performed and the patient was instructed to take a deep breath and hold it. A-V dissociation occurs in the second strip during which time no delta wave is apparent and a definite small Q wave is seen preceding the remainder of the QRS complex. The atria recapture the ventricles in the fourth strip and WPW complexes are again apparent.

tion. Although A-V dissociation following administration of atropine is not uncommon, the development of a true A-V nodal rhythm with retrograde activation of the atria is not frequent. In a review of the literature in which atropine was used in cases of the WPW syndrome, only two other such cases were found.[71,72]

Another example of A-V dissociation with the production of normal appearing QRS complexes is seen in Figure 10. A prominent delta wave is seen in lead I and is less apparent in leads II and III. After atropine was given the subject took a deep breath and A-V dissociation occurred with upright P waves following the QRS complexes, denoting control of the atria by the S-A node. The QRS complexes assumed a normal configuration until atrial recapture of the A-V node occurred.

Normalization after administration of atropine without the presence of A-V dissociation was thought to develop in five subjects. In three it was associated with other maneuvers such as breath-holding, standing and hyperventilation, and in two it resulted from administration of atropine alone.

Many degrees of normalization may occur after administration of atropine and after other procedures. It is often difficult to tell whether or not complete normalization has occurred, particularly if only one lead is being recorded. What appears to be complete normalization in one lead will prove to be only partial normalization or pseudonormalization when simultaneous leads are recorded.

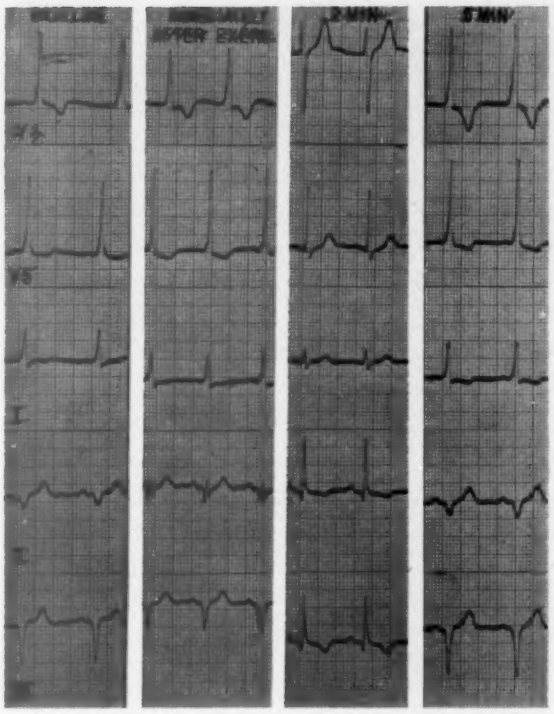


FIG. 16. Exercise test in a subject who demonstrated both a change in the type of WPW conduction and normal complexes during the test. The baseline tracing shows an obvious WPW syndrome. Immediately following exercise a change in the type of anomalous excitation occurred. At two minutes normal conduction was present and at five minutes the electrocardiogram had returned to its baseline appearance.

An example of pseudonormalization is seen in Figure 11A. Twenty seconds after injection of atropine, the QRS complex is less abnormal (Fig. 11B) and at one minute (Fig. 11C) a marked change occurred compared to the baseline tracing, particularly in leads II and III. However, a small but definite delta wave is still apparent in lead I and an abnormal R/S ratio still exists in lead V_2. This is an example of pseudonormalization which might have been classified as complete normalization without simultaneously recording leads.

Effect of Respiratory Maneuvers: Various respiratory maneuvers were carried out in these subjects to determine the effect of vagal stimulation on the WPW syndrome. Vagotonic influences on the heart created by pulmonary stretch reflexes have been previously demonstrated.[73–75] These subjects were subjected to periods of breath-holding, hyperventilation, hyperventilation followed by breath-holding, inhalation of 100 per cent oxygen and pressure breathing. Subjects demonstrating normalization with these procedures represented a much smaller number than with injection of atropine, but several interesting observations were made. In some subjects the onset of each deep inspiration converted the WPW complexes to normal and this change could be produced at will (Fig. 12, A and B). In some the onset of breath-holding was followed by only one or two normally conducted beats or by intermittent normally conducted beats, but with a change back to WPW conduction prior to expiration.

The manner of ventricular excitation in subjects with the WPW syndrome is quite variable. Minor to marked changes may be produced in the configuration of the QRS complexes with such benign maneuvers as increased respiratory excursion, standing and slight exercise. Spontaneous changes in configuration of the QRS complexes may be marked. Variability in ventricular excitation is well known and recently a case was documented in which ten distinct, different patterns of ventricular excitation were described in one person.[76] None of the subjects who were evaluated could be stated to have a completely stable electrocardiogram when attention was given both to the configuration and duration of the delta waves and the remaining QRS complexes. Striking T wave changes were also noted in the majority.

The instability of ventricular conduction was well demonstrated in some subjects by simple breathing maneuvers (Figs. 13 and 14, A, B and C). Striking changes in ventricular conduction is the rule rather than the exception in the WPW syndrome. A-V dissociation with interference developed in three subjects during a period of breath-holding immediately after hyperventilation. During A-V dissociation, when the A-V node was the pacemaker for the ventricles, the QRS complexes appeared normal (Fig. 15). In these subjects A-V dissociation also developed in the immediate period following intravenous administration of atropine.

Vagal influences are important to the intermittent nature of the WPW syndrome, but there is no consistency in the effects of increased or decreased vagal tone in all subjects. Some will convert from anomalous to normal conduction with increased vagal tone, as during breath-holding. Others will convert from normal to the WPW syndrome with the same maneuver. Similar findings were noted with hyperventilation, hyperventilation followed by breath-holding and with exercise both before and following the administration of atropine. The effect of decreased or increased vagal tone depends on its relative influence on the A-V junction and the accessory pathways.

Digitalis and quinidine were not used during this

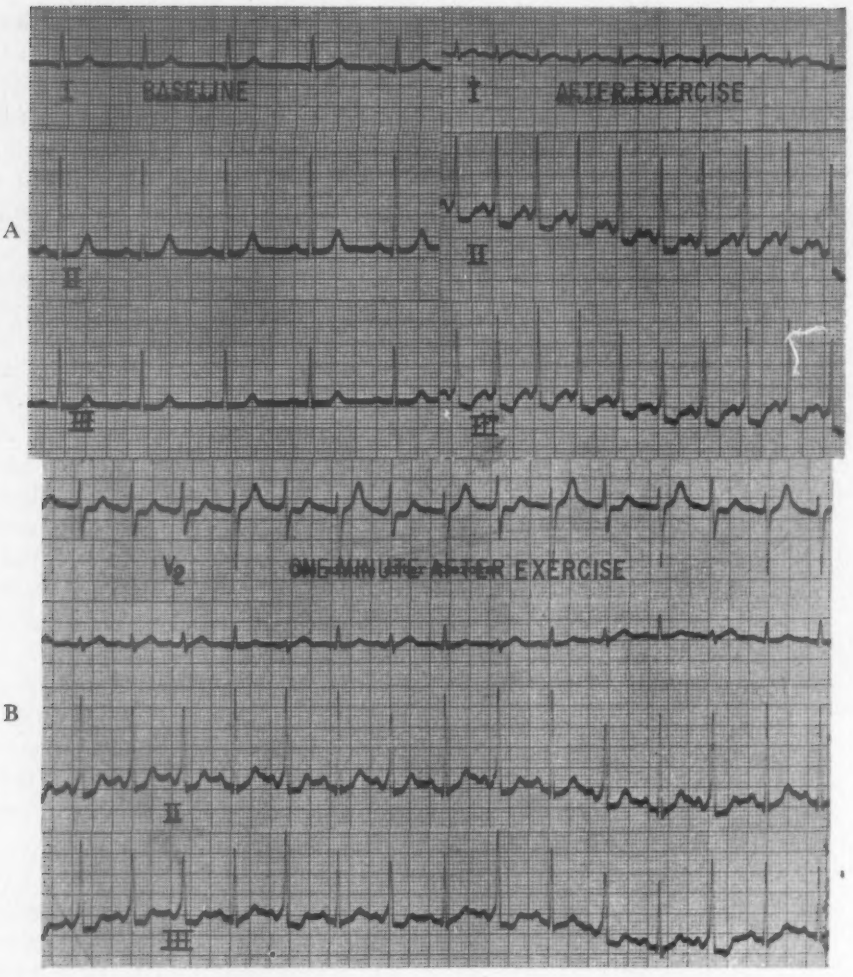


FIG. 17. Effects of exercise tests. A, before and after exercise. After exercise the heart rate approached 150 per minute and definite WPW conduction was present with prominent delta waves. B, one minute following exercise intermittent WPW is present. As the heart rate continues to slow, normal conduction becomes predominant.

investigation, but they have been used experimentally by a number of workers.[23,24,39,71,77–81] It is assumed that digitalis has more of a depressant effect on the normal conduction pathways than on the accessory pathways, allowing more impulses to pass over the accessory pathways, thus increasing anomalous excitation. Quinidine is considered to have a greater affinity for the anomalous pathways; therefore, decreasing the number of impulses passing over them causes less anomalous excitation and, in many instances, normalization.

EXERCISE TEST

A double Master exercise test was performed in sixty subjects. The variability of ventricular conduction in the WPW syndrome accounts for many false positive exercise tests (Fig. 16). This occurred in sixteen subjects (27 per cent). Marked changes in the S-T segment and T waves occurred. This has sometimes been a point of confusion in the evaluation of patients suspected of having coronary artery disease in whom the WPW syndrome was not recognized. Actually, the exercise test is not valid in the face of a baseline abnormal electrocardiogram.

Since exercise has been considered to decrease vagal tone, increasing the likelihood of normal conduction, it has been used in some cases for this purpose. Normal conduction following exercise developed in only two subjects in this series. Of equal interest was a subject in whom the WPW syndrome was present on some days

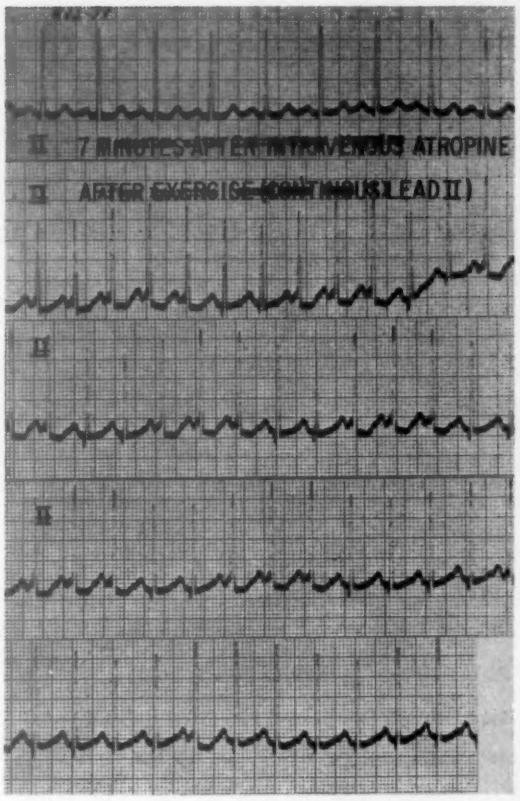


FIG. 18. The same subject as in Figure 17, with exercise seven minutes after administration of atropine. Lead II in the upper strip shows that normal conduction is present; after exercise the WPW conduction appears in an intermittent fashion. This was in spite of markedly reduced vagal tone following administration of atropine which has been thought to decrease the likelihood of the anomalous conduction.

and not on others, and in whom abnormal complexes repeatedly developed after exercise (Figs. 17A and B, and 18).

VECTORCARDIOGRAPHIC ANALYSIS

Vectorcardiographic analysis using an electrically balanced lead system[83–85] was performed in sixty-seven subjects. The electrical forces responsible for the initial slurring of the QRS complexes in these subjects could, for the most part, be distinctly separated from the remaining portion of the QRS loop. These were responsible for the delta wave and were of fairly low amplitude. They were of significant duration and their spatial orientation could be readily determined by inspection of the frontal, transverse and sagittal loops.

Figure 19 shows the frontal, transverse and sagittal loops and the electrocardiogram from a subject in whom the electrical forces responsible for the delta wave were directed downward, to the right and

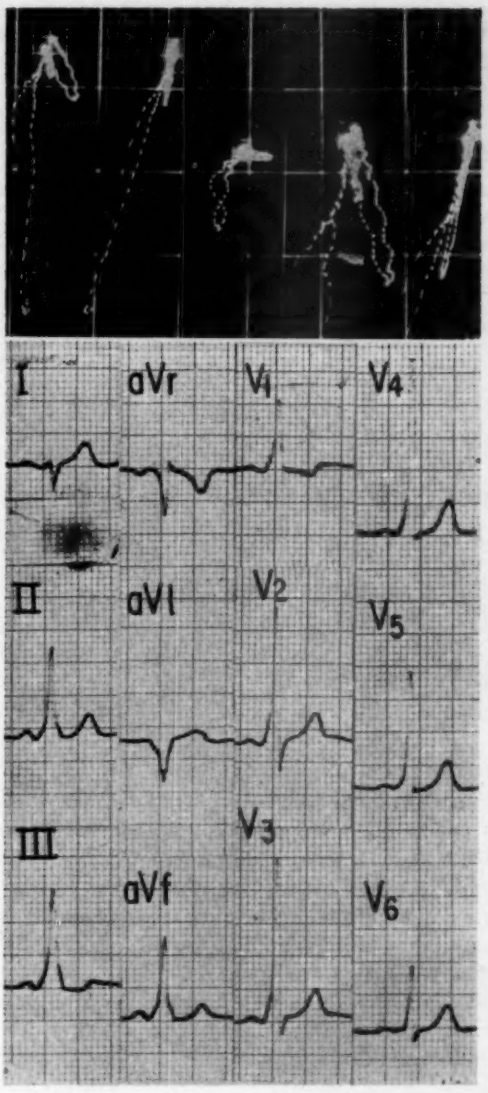


FIG. 19. Vectorcardiogram demonstrating vertical QRS loop orientation. The vectorcardiographic projections from left to right are frontal, sagittal, transverse, enlarged center of frontal and sagittal planes.

anteriorly, with the spatial orientation of the remaining portion of the QRS loop similarly directed. The close approximation of the time markings demonstrates the relatively long duration of the delta wave and the relatively low amplitude of the electrical forces producing it. Occasional subjects show close grouping of the time markers throughout the QRS loop similar to that of left bundle branch block. Such examples probably represent ventricular excitation almost exclusively by the aberrant pathway (Fig. 20).

Figure 21 shows the vectorcardiogram in a subject with the electrical forces responsible for the delta wave directed upward and to the left. Those who showed marked changes in the type of WPW conduction from time to time have vectorcardiograms which present graphic representation of this. In

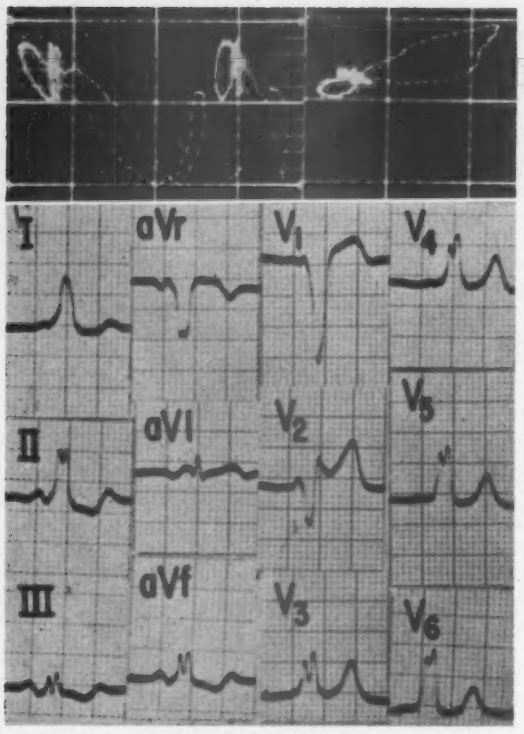


FIG. 20. Vectorcardiogram of a subject with WPW syndrome and extensive anomalous conduction resembling left bundle branch block. The vectorcardiograms from left to right are frontal, sagittal and transverse planes.

Figure 22 are seen the vectorcardiograms of a subject in whom more than one type of anomalous ventricular excitation was present. Both vectorcardiograms show definite evidence of the WPW syndrome, but are quite different from one another in configuration and orientation.

Vectorcardiographic analysis in patients with WPW syndrome is a very useful method for

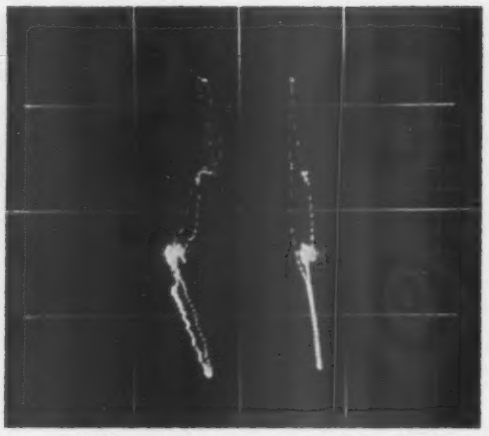


FIG. 21. Vectorcardiogram of a subject with WPW syndrome demonstrating a QRS loop directed headward (frontal plane, left; sagittal plane, right).

determining both the spatial orientation and duration of the electrical forces responsible for the early deformity seen in the QRS complexes of the standard twelve-lead electrocardiogram.

ASSOCIATED ELECTROCARDIOGRAPHIC FINDINGS

In these subjects, as in others without the WPW syndrome, other types of electrocardiographic changes are apt to develop which may or may not be due to organic heart disease. A few such illustrative cases have been reported in the literature, such as associated first degree A-V block, left bundle branch block and right bundle branch block.[72,82,86]

In this series, the following electrocardiographic findings were noted: One subject showed very frequent *nodal premature contractions*. Three showed *atrial premature beats*. The QRS complexes associated with the latter

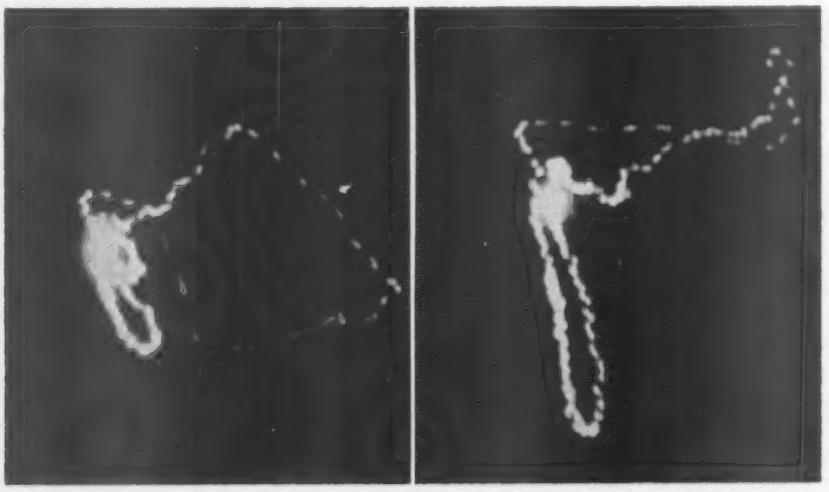


FIG. 22. Frontal plane vectorcardiogram of a subject with WPW syndrome and multiple variations in aberrant ventricular conduction. Two variations are shown.

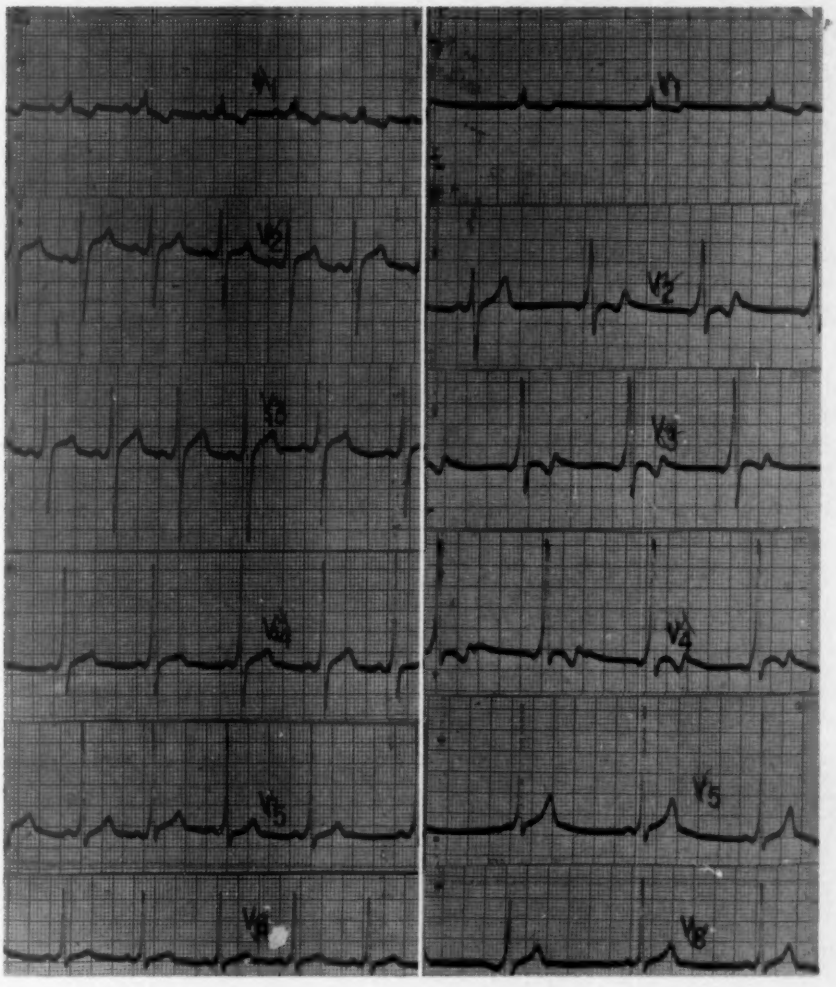


FIG. 23. The V leads demonstrate marked changes in ventricular excitation during atrial rhythm in this subject. See text.

showed no change in one; the other two showed moderate changes in the appearance of the delta wave and remaining QRS complex. Six subjects showed the spontaneous or experimental production of intermittent *atrial rhythm*. No striking changes were noted in the configurations of the QRS complexes during the period of the atrial rhythm except for one subject in whom striking changes were noted, particularly in the precordial leads (Fig. 23). The electrocardiogram of another subject with intermittent atrial rhythm showed little change in the associated QRS complexes (Fig. 24). One subject showed sinus arrest with nodal escape. The QRS complex was normal in the nodal escape beat.

The interesting combination of the WPW syndrome and *parasystole* from a ventricular focus was found in one subject. This combination had previously been reported.[43,87] This twenty-seven year old asymptomatic pilot had no evidence of organic cardiovascular disease. His routine electrocardiogram was diagnostic (Fig. 25A and B). While under observation premature ventricular contractions de-

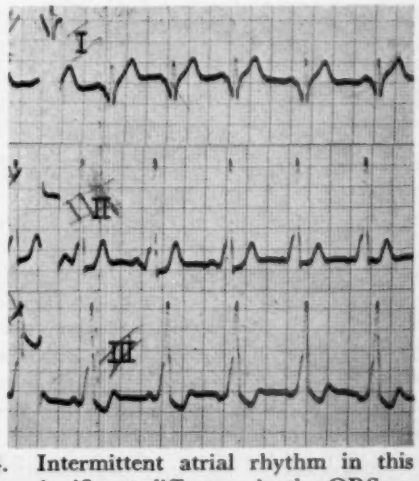


FIG. 24. Intermittent atrial rhythm in this subject caused no significant difference in the QRS complexes.

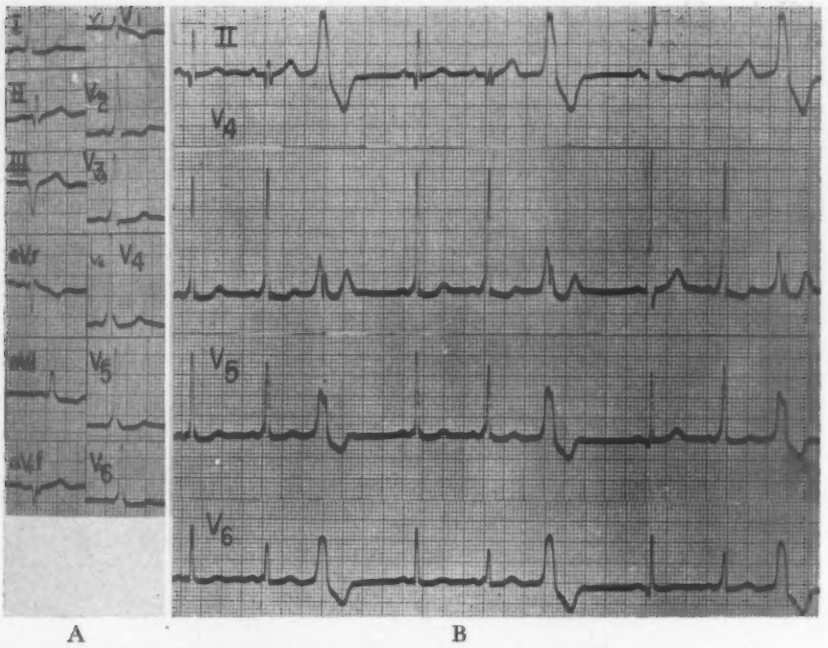


FIG. 25. Ventricular premature beats. A, routine electrocardiogram of a subject with WPW syndrome. B, leads II, V_4, V_5 and V_6 recorded simultaneously demonstrate the WPW syndrome and ventricular premature beats.

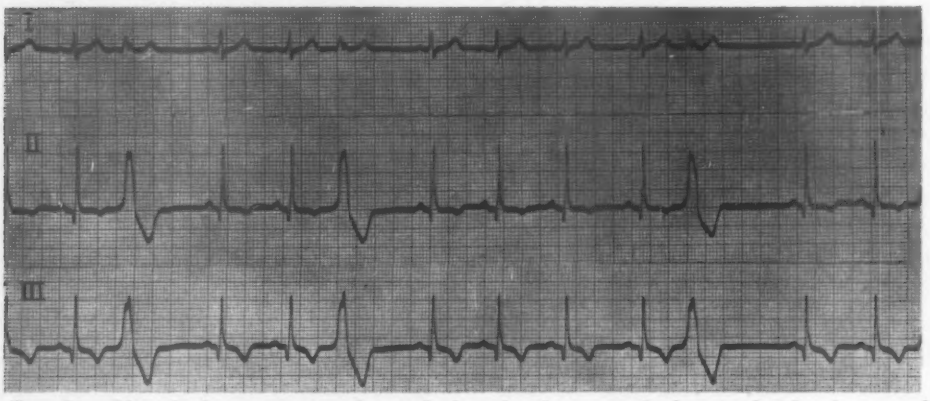


FIG. 26. Ventricular premature beats during the time ventricular conduction is normal. This record is from the same subject as in Figure 25.

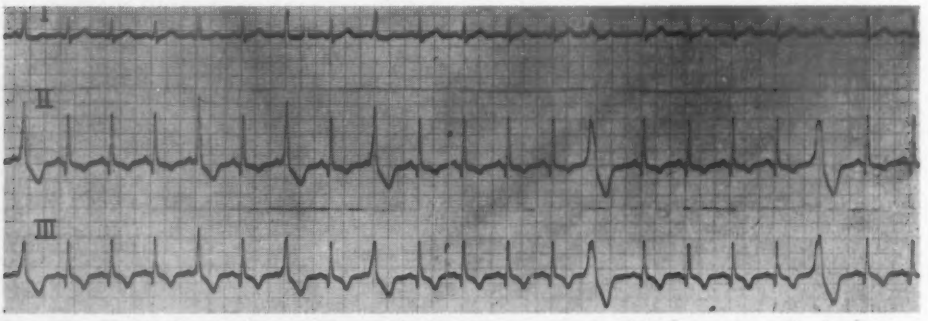


FIG. 27. Variation in degree of ventricular fusion seen in this figure is typical of parasystole. This is the same subject as in Figures 25 and 26.

veloped with varying relationship to the preceding beats and obvious fusion beats. It is of interest that the complexes following the premature beats differ in configuration from those preceding the premature beats, although they still show anomalous atrioventricular excitation. When in normal conduction, the complexes following the premature beats were not different from those preceding them.

(Fig. 26). This points out the relative instability of ventricular conduction when the WPW syndrome is present and the relative stability of ventricular excitation when conduction is normal. Typical fusion beats from a parasystolic ventricular focus were also observed (Fig. 27). Simultaneous leads were recorded on the same subject following administration of atropine when the WPW syndrome was not apparent. Variation in the time of the premature beat to the preceding normal beat and variations in their configuration point to a parasystolic ectopic ventricular focus.

Summary

One hundred nine new cases of the WPW syndrome are presented. One hundred six were discovered as the result of an electrocardiographic survey of 67,375 asymptomatic healthy adult men producing an occurrence rate of 1.6 per thousand.

There was an equal distribution among the various age groups; none was thought to have underlying organic heart disease and the incidence of paroxysmal tachycardia was approximately 12 per cent.

The electrocardiographic characteristics, the instability of intraventricular excitation and the intermittent nature of the anomalous excitation are discussed.

The experimental production of normal excitation is discussed with particular reference to the effects of varying vagal tone at various levels of the conduction system and to the value of intravenous administration of atropine sulfate.

The vectorcardiographic characteristics are presented.

The variability and lability of the S-T segments and T waves are stressed with respect to both spontaneous changes and those following various maneuvers.

The probable congenital nature of the true WPW syndrome is stressed and the usual benign clinical nature discussed. This study casts serious doubt on the concept of an acquired WPW syndrome.

References

1. Wolff, L., Parkinson, J. and White, P. D. Bundle branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. *Am. Heart J.*, 5: 685, 1930.
2. Öhrnell, R. F. Pre-excitation. A cardiac abnormality. *Acta med. scandinav.* (supp. 152), p. 13, 1944.
3. Rosenbaum, F. F., Hecht, H. H., Wilson, F. N. and Johnston, F. D. The potential variations of the thorax and the esophagus in anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 29: 281, 1945.
4. Prinzmetal, M., Kennamer, R., Corday, E., Osborne, J. A., Fields, J. and Smith, L. A. Accelerated Conduction. The Wolff-Parkinson-White Syndrome and Related Conditions, p. 1. New York, 1952. Grune & Stratton.
5. Wilson, F. N. A case in which the vagus influenced the form of the ventricular complex of the electrocardiogram. *Arch. Int. Med.*, 16: 1008, 1915.
6. Wedd, A. M. Paroxysmal tachycardia with reference to normotopic tachycardia and the role of the extrinsic cardiac nerves. *Arch. Int. Med.*, 27: 571, 1921.
7. Bain, C. W. C. and Hamilton, C. K. Electrocardiographic changes in rheumatic carditis. *Lancet*, 1: 807, 1929.
8. Hamburger, W. W. Bundle branch block. Four cases of intraventricular block showing some interesting and unusual clinical features. *M. Clin. North America*, 13: 343, 1929.
9. Newman, M. Bundle branch block of vagal origin. *Brit. M. J.*, 2: 1134, 1931.
10. Wolferth, C. C. and Wood, F. C. The mechanism of production of short P-R intervals and prolonged QRS complexes in patients with presumably undamaged hearts: hypothesis of an accessory pathway of auriculoventricular conduction (bundle of Kent). *Am. Heart J.*, 8: 297, 1933.
11. Holzmann, M. and Scherf, D. Über Elektrokardiogramme mit verkurzter Vorhof-Kammer-Distanz und positiven P-Zacken. *Ztschr. Klin. Med.*, 121: 404, 1932.
12. Kent, A. F. Observations on the auriculo-ventricular junction of the mammalian heart. *Quart. J. Exper. Physiol.*, 7: 193, 1914.
13. Glomset, T. J. and Glomset, A. T. A. A morphologic study of the cardiac conduction system in ungulates, dogs and man. I. The sinoatrial node. *Am. Heart J.*, 20: 309, 1940.
14. Kistin, A. D. Observations on the anatomy of the atrioventricular bundle (bundle of His) and the question of other muscular atrioventricular connections in normal human hearts. *Am. Heart J.*, 37: 849, 1949.
15. Lev, M. and Lerner, R. The theory of Kent. A histologic study of the normal atrioventricular communications of the human heart. *Circulation*, 12: 176, 1955.
16. Mahaim, I. and Winston, M. R. Recherches d'anatomie compareé et de pathologie experimentale sur les connexions hautes du jaisceau de His-Tawara. *Cardiologia*, 5: 189, 1941.
17. Mahaim, I. Kent fibers and the A-V paraspecific conduction through the upper connections of the bundle of His-Tawara. *Am. Heart J.*, 33: 651, 1947.
18. Butterworth, J. S. and Poindexter, C. A. Short P-R interval associated with a prolonged QRS complex—a clinical and experimental study. *Arch. Int. Med.*, 69: 437, 1942.
19. Wood, F. C., Wolferth, C. C. and Geckeler, G. D. Histologic demonstration of accessory muscular connections between auricle and ventricle in a case of short P-R interval and prolonged QRS complex. *Am. Heart J.*, 25: 454, 1943.

20. Hecht, H. H., Kennamer, R., Prinzmetal, M., Rosenbaum, F. F., Sodi-Pallares, D., Wolff, L., Brooks, C., Peck, A., Rijlant, P. and Robb, J. S. Anomalous atrioventricular excitation—panel discussion. *Ann. New York Acad. Sc.*, 65: 826, 1957.
21. Bishop, L. F. Bundle branch block with short P-R interval in individuals without organic heart disease. *Am. J. M. Sc.*, 194: 794, 1947.
22. Hunter, A., Papp, C. and Parkinson, J. The syndrome of short P-R interval, apparent bundle branch block and associated paroxysmal tachycardia. *Brit. Heart J.*, 2: 107, 1940.
23. Pearson, J. R. and Wallace, A. W. The syndrome of paroxysmal tachycardia with short P-R interval and prolonged QRS complex with report of two cases. *Ann. Int. Med.*, 21: 830, 1944.
24. Movitt, E. R. Some observations on the syndrome of short P-R interval with long QRS. *Am. Heart J.*, 29: 78, 1945.
25. Stein, I. Short P-R interval, prolonged QRS complex (Wolff-Parkinson-White syndrome); report of 14 cases and a review of the literature. *Ann. Int. Med.*, 24: 60, 1946.
26. Lenzi, S. On the Wolff-Parkinson-White syndrome. *Cuore e circolaz.*, 31: 141, 1947.
27. Goldberg, H. H. and Lewis, S. M. Acute myocardial infarction and the Wolff-Parkinson-White syndrome. *Am. Heart J.*, 40: 614, 1950.
28. Scherf, D., Blumenfeld, S. and Mueller, P. A-V conduction disturbance in the presence of the pre-excitation syndrome. *Am. Heart J.*, 43: 829, 1952.
29. Langendorf, R., Lev, M. and Pick, R. Auricular fibrillation with anomalous A-V excitation (WPW syndrome) imitating ventricular paroxysmal tachycardia. *Acta cardiol.*, 7: 241, 1952.
30. Kossmann, C. E., Berger, A. R., Butter, S. A., Rader, B. and Brümlik, J. Anomalous atrioventricular excitation produced by catheterization of the normal human heart. *Circulation*, 1: 902, 1950.
31. Sodi-Pallares, D., Soberon, J., Thomsen, P., Fishleder, B. L. and Estandia, A. Contribucion al estudio del sindrome de W.P.W. por las derivaciones intracavitarias. *Arch. Inst. cardiol. Mexico*, 18: 1, 1948.
32. See reference 4.
33. Sodi-Pallares, D. and Calder, R. M. New Bases of Electrocardiography. St. Louis, 1956. C. V. Mosby Co.
34. Malinow, M. R. and Langendorf, R. Different mechanisms of fusion beats. *Am. Heart J.*, 35: 448, 1948.
35. Peck, A. Parasystole. *Circulation*, 8: 243, 1953.
36. Hoffman, I., Morris, M. H., Friedenfeld, L. and Gittler, D. Aberrant beats of Wolff-Parkinson-White configuration in arteriosclerotic heart disease. *Brit. Heart J.*, 18: 301, 1956.
37. Lown, B., Ganong, W. F. and Levine, S. A. The syndrome of short P-R interval, normal QRS complex and paroxysmal rapid heart action. *Circulation*, 5: 693, 1952.
38. Kaplan, G. and Cohn, T. D. Syndrome of auriculoventricular accessory pathway. *Ann. Int. Med.*, 21: 824, 1944.
39. Littman, D. and Tarnover, H. Wolff-Parkinson-White syndrome—a clinical study with report of 9 cases. *Am. Heart J.*, 32: 100, 1946.
40. Reed, J. C., Langley, R. W. and Utz, D. C. A review of 8 cases of Wolff Parkinson-White syndrome including 4 cases with initial left ventricular activation as demonstrated by the multiple precordial leads (Abstract). *Am. Heart J.*, 33: 701, 1947.
41. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1,000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
42. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew. *Circulation*, 10: 401, 1954.
43. Hejtmancik, M. R. and Herrmann, G. R. The electrocardiographic syndrome of short P-R interval and broad QRS complexes: a clinical study of 80 cases. *Am. Heart J.*, 54: 708, 1957.
44. Bodlander, J. W. The Wolff-Parkinson-White syndrome in association with congenital heart disease: coarctation of the aorta. *Am. Heart J.*, 31: 785, 1946.
45. Kimball, J. L. and Burch, G. The prognosis of the Wolff-Parkinson-White syndrome. *Ann. Int. Med.*, 27: 239, 1947.
46. Richmond, J. B., Moore, H. R. and Callen, I. R. The Wolff-Parkinson-White syndrome in an infant. *Pediatrics*, 1: 635, 1948.
47. Schieve, J. F. Paroxysmal tachycardia in an infant with Wolff-Parkinson-White syndrome. *Am. J. Dis. Child.*, 77: 474, 1949.
48. Gleckler, W. J. and Lay, J. V. M. Wolff-Parkinson-White syndrome and paroxysmal tachycardia in infancy. *J. A. M. A.*, 150: 683, 1952.
49. Paul, O. and Harrison, C. J., Wolff-Parkinson-White syndrome in an infant. *J. A. M. A.*, 149: 363, 1952.
50. Kriedberg, M. B. and Dushan, T. A. Paroxysmal auricular tachycardia associated with Wolff-Parkinson-White syndrome in a newborn infant. *J. Pediat.*, 43: 92, 1953.
51. McIntire, M. S. and Freed, A. E. The Wolff-Parkinson-White syndrome. Report of a case in a mother and infant. *Am. J. Dis. Child.*, 89: 743, 1955.
52. Averill, K. H. Wolff-Parkinson-White syndrome occurring in brothers. *Am. Heart J.*, 51: 943, 1956.
53. Harnischfeger, W. W. Hereditary occurrence of the pre-excitation (WPW) syndrome with re-entry mechanism and concealed conduction. *Circulation*, 19: 28, 1959.
54. Wolff, L. and White, P. D. Syndrome of short P-R interval with abnormal QRS complexes and paroxysmal tachycardia. *Arch. Int. Med.*, 82: 446, 1948.
55. Schiebler, G. L., Adams, P., Anderson, R. C., Amplatz, K. and Lister, R. G. Clinical study of twenty-three cases of Ebstein's anomaly of the tricuspid valve. *Circulation*, 19: 165, 1959.
56. Willius, F. A. and Carryer, H. M. Electrocardiograms displaying short P-R intervals with prolonged QRS complexes: an analysis of sixty-five cases. *Proc. Staff Meet. Mayo Clin.*, 21: 438, 1946.
57. Sprague, H. B. Auricular fibrillation and bundle branch block in an apparently normal heart: a case report. *Internat. Clin.*, 1: 186, 1937.
58. Levine, S. A. and Beeson, P. B. The Wolff-

Parkinson-White syndrome with paroxysmal ventricular tachycardia associated with short P-R interval and prolonged QRS complexes. *Ann. Int. Med.*, 24: 911, 1946.

59. Missal, M. E., Wood, D. J. and Lev, S. D. Paroxysmal ventricular tachycardia associated with short P-R interval and prolonged QRS complexes. *Ann. Int. Med.*, 24: 911, 1946.
60. Cain, E. F. Wolff-Parkinson-White syndrome presenting certain unusual features. *Am. Heart J.*, 33: 523, 1947.
61. Wolff, L. Syndrome of short P-R interval with abnormal QRS complexes and paroxysmal tachycardia (Wolff-Parkinson-White syndrome). *Circulation*, 10: 282, 1954.
62. Hubbard, J. P. Paroxysmal tachycardia and its treatment in young infants. *Am. J. Dis. Child.*, 61: 687, 1941.
63. White, P. D., Leach, E. E. and Foote, S. A. Errors in measurement of the P-R (P-Q) interval and QRS duration in the electrocardiogram. *Am. Heart J.*, 22: 321, 1941.
64. Burch, G. E. and Kimball, J. L. Notes on the similarity of QRS complex configuration in the Wolff-Parkinson-White syndrome. *Am. Heart J.*, 32: 560, 1946.
65. Tung, C.-L. Functional bundle branch block. *Am. Heart J.*, 11: 89, 1936.
66. Master, A. M., Jaffe, H. L. and Dack, S. Atypical bundle branch block with short P-R interval in Graves' disease. *J. Mt. Sinai Hosp.*, 4: 100, 1937.
67. Goldman, I. R., Cosby, R. S. and Griffith, G. C. The effect of atropine on the cardiac mechanism in anomalous atrioventricular conduction. *Am. Heart J.*, 40: 903, 1940.
68. Duthie, R. J. Mechanism of the Wolff-Parkinson-White syndrome. *Brit. Heart J.*, 8: 96, 1946.
69. Boe, J. and Tschudi, M. S. Paroxysmal tachycardia and functional bundle branch block in an infant with W-P-W symdrome of type II. *Acta med. scandinav.* (supp. 719), 156: 92, 1956.
70. Averill, K. H. and Lamb, L. E. Less commonly recognized actions of atropine on cardiac rhythm. *Am. J. M. Sc.*, 237: 304, 1959.
71. Fox, T. T. Aberrant atrioventricular conduction in a case showing a short P-R interval and an abnormal but not prolonged QRS complex. *Am. J. M. Sc.*, 209: 199, 1945.
72. Wolff, L. and Richman, J. L. The diagnosis of myocardial infarction in patients with anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 45: 545, 1953.
73. Wilson, F. N. The production of A-V rhythm in man after the administration of atropine. *Arch. Int. Med.*, 16: 989, 1915.
74. Lamb, L. E., Dermksian, G. and Sarnoff, C. A. Significant cardiac arrhythmias induced by common respiratory maneuvers. *Am. J. Cardiol.*, 2: 563, 1958.
75. Dermksian, G. and Lamb, L. E. Cardiac arrhythmias in experimental syncope. *J. A. M. A.*, 168: 1623, 1958.
76. Lamb, L. E. Multiple variations of WPW conduction in one subject. Intermittent normal conduction and a false positive exercise tolerance test. *Am. J. Cardiol.*, 4: 346, 1959.
77. Scherf, D. and Schönbrunner, E. Beiträge zum Problem der verkürzten Vorhofkammerleitung. *Ztschr. klin. Med.*, 128: 750, 1935.
78. Roberts, G. H. and Abramson, D. I. Ventricular complexes of the bundle block type associated with short P-R intervals. *Ann. Int. Med.*, 9: 983, 1936.
79. Wolferth, C. C. and Wood, F. C. Further observations on the mechanism of the production of a short P-R interval in association with prolongation of the QRS complex. *Am. Heart J.*, 22: 450, 1941.
80. Fox, T. T., Travell, J. and Molofsky, L. Action of digitalis on conduction in the syndrome of short P-R interval and prolonged QRS complex. *Arch. Int. Med.*, 71: 206, 1943.
81. Fox, T. T. and Bobb, A. L. On the mechanism of the electrocardiographic syndrome of short P-R interval with prolonged QRS complex. *Am. Heart J.*, 28: 311, 1944.
82. Pick, A. and Katz, L. N. Disturbances of impulse formation and conduction in the pre-excitation (WPW) syndrome—their bearing on its mechanism. *Am. J. Med.*, 19: 759, 1955.
83. Smith, G. B., Jr. and Lamb, L. E. The comparative vectorgram: a single method for analysis of lead similarity. *Am. J. M. Sc.*, 237: 434, 1959.
84. Lamb, L. E. and Smith, G. B., Jr. A study of the human torso as a volume conductor by comparative vectorgram analysis: the dR factor. *Am. J. M. Sc.*, 237: 612, 1959.
85. Lamb, L. E. and Smith, G. B., Jr. An electrically balanced bipolar vectorcardiographic system: lead analysis using the dR factor. *Am. J. M. Sc.*, 237: 759, 1959.
86. Pick, A., and Fisch, C. Ventricular pre-excitation (WPW) in the presence of bundle branch block. *Am. Heart J.*, 55: 504, 1958.
87. Eichert, H. Wolff-Parkinson-White syndrome simulating myocardial infarction. *Ann. Int. Med.*, 21: 907, 1944.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

V. Left Bundle Branch Block*

LAWRENCE E. LAMB, M.D., F.A.C.C., CAPT. KELVIN D. KABLE, MC, USAF *and* CAPT. KEITH H. AVERILL, MC, USAF

San Antonio, Texas

ALTHOUGH it is generally accepted that right bundle branch block may occur as a congenital finding or exist without cardiac disease, it is doubtful if the same can be said regarding left bundle branch block. This paper will examine critically a number of reports relative to the significance of left bundle branch block as well as present data on thirteen examples of complete left bundle branch block found as a result of a routine electrocardiogram in an asymptomatic population of 67,375 subjects. An additional twelve cases of left bundle branch block occurring in the flying population are included. The latter were not found as a result of the routine electrocardiographic survey.

HISTORICAL REVIEW

It is not the intent of this paper to present an exhaustive review of the literature on bundle branch block. A complete review of the literature preceding 1950 has been published by Rosenman, Pick and Katz.[1] In 1938, Yater[2] also published an excellent review and reported cases correlated with pathologic studies. Accordingly, only the highlights of reports that have a direct bearing on the cause and significance of left bundle branch block will be included.

Graybiel and Sprague[3] reported an analysis of 395 cases of bundle branch block. This report greatly influenced the earlier clinical impression that bundle branch block was associated with a poor prognosis. Of this series, on a follow-up evaluation, 223 had died with an average duration of life of fourteen months after the diagnosis of bundle branch block had been made. Undoubtedly, the poor prognosis was a reflection of the underlying serious cardiac disease that prompted medical evaluation and is unrelated to the prognosis of bundle branch block found in an asymptomatic population.

Langley, Reed and Utz[4] reviewed 100 cases of bundle branch block among 6,900 patients of a U. S. Navy Hospital. Owing to the brevity of the report, it is difficult to evaluate part of the conclusions or interpret the significance of left bundle branch block. The authors stated that the prognosis in right bundle branch block was not as grave as that in left bundle branch block. At least five patients with left bundle branch block had myocardial infarction.

Intermittent left bundle branch block has been frequently reported, most often in the presence of recognized heart disease. Comments relative to intermittent bundle branch block have been previously reported.[5]

Following the initial poor prognosis reported for left bundle branch block other reports have indicated that this was not always true. However, a careful review of the reported cases does not permit the extension of this concept to mean that cardiac disease is not present. Wolfram[6] reported seventeen cases of left bundle branch block found in 5,000 electrocardiograms among veterans. He stated that seven of these subjects did not have heart disease; however, some doubt may be expressed concerning the validity of this conclusion when the published case summaries are reviewed.

Vazifdar and Levine[7] published a report

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

which included four patients with left bundle branch block. They were between forty-three and seventy-one years of age and were followed up for an average of ten years (seven to twelve years) without complication. It is doubtful that these four cases of left bundle branch block occurring past the age of forty could be used as indicating a congenital origin of the defect. In addition, the subsequent follow up for a period of seven to twelve years does not have any real bearing on the etiology of left bundle branch block. It is not unusual to see patients with frank myocardial infarction followed up from seven to twelve years without complication.

Manning[8] has reported one case of complete left bundle branch block detected in a survey of 5,000 electrocardiograms from the Royal Canadian Air Force flying population, and apparently no other evidence of cardiac disease could be detected. Packard and associates[9] reported one case of complete left bundle branch block found in conjunction with their evaluation of 1,000 electrocardiograms in Navy pilots during the Second World War. This particular patient has been followed up for a number of years without apparent complication.

Kremer and Delchevalerie[10] reported a familial occurrence of cardiomegaly in three siblings, one of whom had complete left bundle branch block. Although this report is interesting, the presence of cardiomegaly indicating underlying cardiovascular disease suggests that bundle branch block was not the only cardiac disease present, and that a simple isolated occurrence of congenital left bundle branch block was not the case.

Material and Methods

Routine electrocardiograms were recorded on 67,375 members of the flying population in the U. S. Air Force. All were recorded at the time of the annual physical examination. Analysis of these records revealed that thirteen subjects had complete left bundle branch block. Ten of these were evaluated in detail at the School of Aviation Medicine. These thirteen cases comprise Series A and provide a statistical incidence of left bundle branch block in the routine electrocardiographic survey. In addition to these cases, another group of subjects, included as Series B, represent cases of left bundle branch block found in the flying population as a result of electrocardiograms recorded for reasons other than the survey of the asymptomatic flying population. This important series is included as it sheds a great deal of light upon the significance and etiology of left bundle branch block.

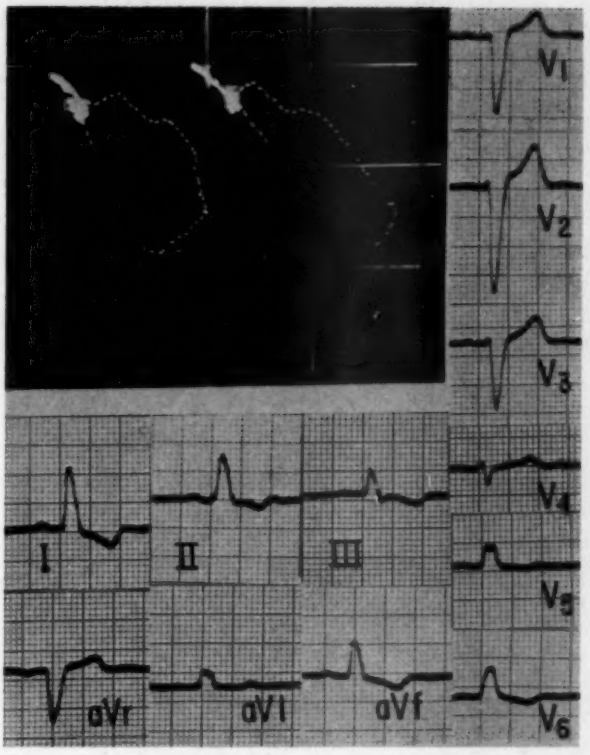


Fig. 1. Case 2. The typical features of left bundle branch block are demonstrated by the routine electrocardiogram. The vectorcardiogram as seen in the frontal (*left*) and sagittal (*right*) views demonstrates a QRS loop directed leftward and posterior. No anterior component to the QRS loop is present. The T loop is directed opposite to the QRS loop.

Clinical evaluation included detailed history, physical examination, routine twelve-lead electrocardiogram, double Master exercise test, vectorcardiograms, various stress procedures, cardiac fluoroscopy and routine laboratory studies, including blood sugar and blood cholesterol levels.

Results and Case Reports

Series A

The incidence of complete left bundle branch block in the asymptomatic population in this study was 0.02 per cent or 1 in 5,000. The average age of the group was thirty-two years. Because of the limited number of such reports available, the case reports are briefly summarized.

Case 1. J. E., twenty-seven years old, was asymptomatic when a routine electrocardiogram demonstrated complete left bundle branch block. At age twelve he was critically ill with rheumatic fever. The illness was of such severity that he was not expected to live and the last rites were administered.

However, he did recover. He passed a flying physical at age twenty-one and no mention of cardiac findings was made prior to a recording of the routine electrocardiogram which demonstrated complete left bundle branch block. The physical examination was within normal limits. The subject was 6 feet, 3 inches in height and weighed 164 pounds. Blood pressure was 122/72 mm. Hg and pulse was 78 per minute. There was a grade 1 apical systolic murmur present.

Comment: This is an example of a young man who had previously experienced rheumatic carditis of sufficient severity to cause complete left bundle branch block. The conduction defect is residual evidence of previous rheumatic carditis in an asymptomatic subject with no abnormal physical findings.

CASE 2. L. C., twenty-eight years old, was asymptomatic when an electrocardiogram demonstrating complete left bundle branch block was recorded (Fig. 1). He had had a severe undiagnosed febrile illness during his first year of life. At age fifteen he had Bright's disease with marked edema and severe hypertension. Following recovery from the one acute episode he had no recurrence of the symptoms or findings referable to renal pathology. Physical examintion was not remarkable.

Comment: This is another example of a young man who presents with complete left bundle branch block and a past history of a serious illness. The left bundle branch block was likely a result of myocarditis associated with the streptococcal infection preceding glomerulonephritis or secondary to vascular disease associated with glomerulonephritis.

CASE 3. L. M., thirty-eight years old, was asymptomatic when complete left bundle branch block was noted on a routine electrocardiographic tracing. Past and family histories were non-contributory. Physical examination revealed a healthy young man, 5 feet, 10 inches tall and weighing 193 pounds. He exhibited a tendency to vascular hyperreactivity. The initial blood pressure recording was 152/106 mm. Hg, while subsequent determinations were within normal limits, being recorded as low as 128/74 mm. Hg.

Comment: Complete medical evaluation and past history of this subject failed to reveal any etiology for the origin of complete left bundle branch block. If any previous infectious disease occurred to cause carditis, it was unknown or denied by the patient. Numerous electrocardiograms were recorded at different medical facilities; all showed complete left bundle branch block. A follow-up evaluation

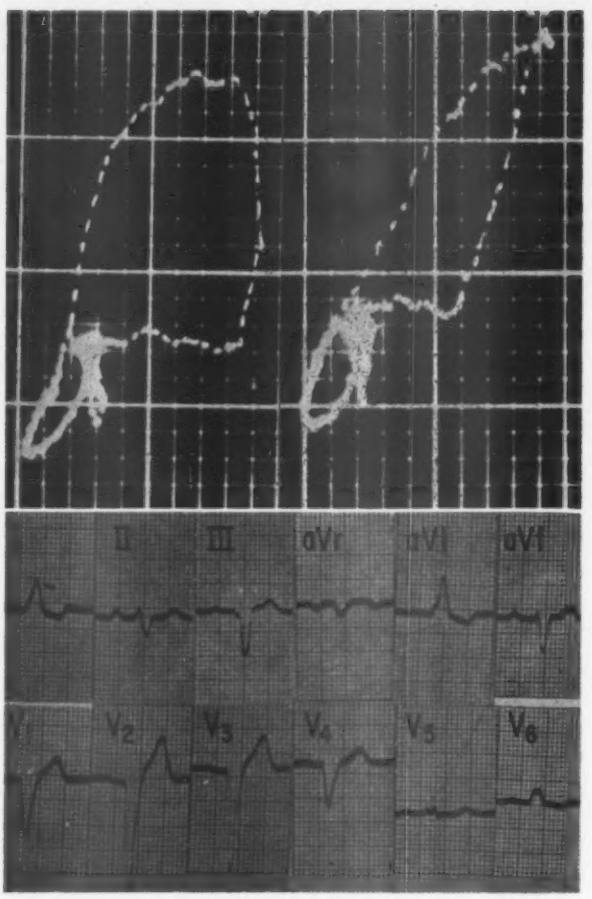


FIG. 2. Case 4. An example of left bundle branch block with the QRS loop directed upward. The frontal (*left*) and sagittal (*right*) views are depicted. The QRS loop is counterclockwise in both projections and no anterior component is noted.

sixteen months after the initial record of left bundle branch block demonstrated a normal electrocardiogram. After exercise with an increased cardiac rate, complete block was again noted. As the rate slowed, intermittent block occurred. The demonstration of intermittent left bundle branch block strongly suggests abnormality of the conduction system rather than a congenital defect.

CASE 4. O. A. was an asymptomatic twenty-nine year old officer found to have complete left bundle branch block (Fig. 2). His past illnesses included measles, mumps and chicken pox with an occasional infection of the upper respiratory tract. He was hospitalized in 1945 for a few days because of a mild sore throat and fever. The family history was non-contributory other than the fact that all of his grandparents lived until their eighth decade. Physical examination was unremarkable, revealing a young officer of healthy appearance, 5 feet, 8½ inches in height, weighing 156 pounds.

Comment: It is not possible to pinpoint any particular acute illness as the cause of complete left bundle branch block in this subject. The possibility that the sore throat and fever for which he was hospitalized in 1945 caused myocarditis cannot be excluded.

CASE 5. N. G. was a thirty-six year old officer in apparent good health and asymptomatic when he was found to have complete left bundle branch block. Eleven years before an electrocardiogram had been recorded which was not available for comparison. He was told at that time that his electrocardiogram was unusual. The family history was non-contributory. Physical examination revealed that he was 6 feet tall, weighed 167 pounds, and had a blood pressure of 122/70 mm. Hg. There was a grade 2 apical systolic murmur. On fluoroscopic examination he presented the interesting finding of a leiomyoma of the esophagus. This was subsequently removed by operation without complications. Cardiac catheterization was also performed and the results were within normal limits.

Comment: No etiology for complete left bundle branch block is apparent. It is doubtful that the presence of the leiomyoma of the esophagus has any direct relationship to the occurrence of left bundle branch block.

CASE 6. D. A. was an asymptomatic thirty-six year old officer found to have complete left bundle branch block on a routine electrocardiogram. His past history was significant in that he had had severe diphtheria at the age of six. Convalescence required more than a month. There were no known sequelae. The family history was non-contributory. On physical examination the patient was of healthy appearance, 5 feet, $8^1/_2$ inches in height and 160 pounds in weight. There were no other significant findings.

Comment: The presence of severe diphtheria in childhood suggests the possibility that the conducting system of the heart was involved and left bundle branch block may have occurred as a direct result of diphtheritic myocarditis.

CASE 7. H. V., an asymptomatic thirty-six year old officer, was found to have complete left bundle branch block on a routine electrocardiogram. His past history included chicken pox at the age of six, and bronchial pneumonia at five years of age. The family history was non-contributory. Physical examination revealed a muscular, balding, middle-aged appearing man, 5 feet, 7 inches in height and 148 pounds in weight. The blood pressure was 120/84 mm. Hg. There were no other significant findings.

Comment: It is not possible to state the etiology of the left bundle branch block in this case. The physical appearance of a muscular, balding, middle-aged man tends to favor a diagnosis of underlying coronary disease. On the other hand, pneumonia at age five may have been a significant fact and could have been associated with inflammatory changes of the conduction system.

CASE 8. R. S. was a thirty-eight year old officer who was found to have complete left bundle branch block on a routine electrocardiogram. His past history revealed only measles as a child, and hospitalization for influenza while in the Army. In 1951 he experienced an episode of syncope during warm weather which was associated with clinical symptoms suggestive of acute labyrinthitis, manifested by several weeks of dizziness, marked nausea and vomiting. After treatment the symptoms cleared and there were no subsequent difficulties. His mother died of a stroke as a complication of long standing hypertension. The other interesting feature of his history was the presence of intermittent ringing in both ears which was not persistent or troublesome. Physical examination revealed a man of healthy appearance, 5 feet, 8 inches tall and weighing 150 pounds. The blood pressure was 122/64 mm. Hg. There was slight premature graying of the hair. No other significant physical findings were noted. He was evaluated over a year after left bundle branch block was first observed and no complications had occurred in the intervening time.

Comment: The etiology of left bundle branch block in this case must remain obscure in the absence of significant past history or sufficient clinical evidence to substantiate the presence of any active disease processes.

CASE 9. L. S. was an asymptomatic officer in whom complete left bundle branch block was discovered on a routine examination at age thirty-eight. His past history included vague discomfort in the upper abdomen, and excessive belching approximately two years before. The family history was interesting in that his mother died at age fifty of a cerebral hemorrhage following renal disease, one maternal uncle died of a heart attack and another maternal uncle died of a stroke. Physical examination revealed a man of healthy appearance 5 feet, 9 inches tall and 144 pounds in weight. The blood pressure was 124/88 mm. Hg.

Comment: The origin of left bundle branch block in this subject remains obscure. The episode of acute indigestion at age thirty-six may have been more than indigestion; however, there was no clinical information to support a more definitive diagnosis. A complete upper gastrointestinal x-ray study performed at

TABLE I

Electrocardiographic and Vectorcardiographic Features in Thirteen Cases of Left Bundle Branch Block (Series A)

Case No.	Heart Rate (per min.)	P-R Interval (sec.)	QRS Duration (sec.)	Q-T Interval (sec.)	Mean QRS Vector	Mean T Vector	Heart Rate During Exercise (per min.)			Vectorcardiographic QRS Loop
							Before	Immediately After	Two Minutes After	
1	64	0.18	0.13	0.44	−30° posterior; transition at lead V_5	+60° anterior; upright in leads V_1 to V_6	72	96	55	No anterior component
2	70	0.18	0.13	0.44	+45° posterior; transition at lead V_3	−105° anterior; transition at lead V_4	48	70	50	No anterior component
3	75	0.18	0.14	0.40	+45° posterior; transition at lead V_4	+60° anterior; upright in leads V_1 to V_6	78	100	92	No anterior component
4	78	0.18	0.14	0.40	0° posterior; transition at lead V_6	+90° anterior; upright in leads V_1 to V_6	..	..	..	..
5	84	0.18	0.14	0.42	−30° posterior; transition at lead V_4	+90° anterior; transition at lead V_6	72	110	75	No anterior component
6	80	0.14	0.14	0.38	+60° posterior; transition at lead V_3	+60° anterior; transition at lead V_6	75	100	75	No anterior component
7	75	0.12	0.14	0.42	+60° posterior; transition at lead V_3	+60° anterior; transition at lead V_6	70	80	72	No anterior component
8	70	0.16	0.16	0.44	0° posterior; transition between leads V_3 and V_4	+75° anterior; upright in leads V_1 to V_6	60	100	72	No anterior component
9	75	0.18	0.16	0.42	−45° posterior; transition between leads V_4 and V_5	+75° anterior; transition at lead V_6	60	75	60	Anterior component present
10	78	0.16	0.12	0.38	+60° posterior; transition at lead V_4	+60° anterior; transition at lead V_5	..	..	..	No anterior component
11	55	0.16	0.12	0.44	+30° posterior; transition between leads V_5 and V_6	+30° anterior; transition at lead V_6	..	..	..	..
12	75	0.14	0.14	0.44	+45° anterior; transition at lead V_4	+60° anterior; transition between leads V_4 and V_5	..	..	..	..
13	80	0.20	0.14	0.42	0° posterior; transition at lead V_4	+80° anterior; transition at lead V_5	..	..	..	No anterior component

the time of symptoms revealed no abnormalities but no electrocardiogram was taken.

CASE 10. T. B. was a forty year old officer found to have complete left bundle branch block during a routine electrocardiogram. Periodically during the past two years, this patient had noted bilateral aching pain in the area about the angle of the jaw and extending posteriorly around the neck to the midline and down the anterior part of the neck to the clavicle. This pain was most severe on the left side and generally occurred in the evening. It would not appear during exercise, but often occurred one to two hours following exercise. There was no associated pain in the chest or other symptoms. Previous roentgenographic examination revealed reversal of the normal lordotic curve of the cervical spine and narrowing of the interspaces between C4, C5 and C6. There was no other symptomatology which might be construed as referable to the cardiovascular system. His past history was significant in that he had scarlet fever during childhood. He also had malaria during World War II with one recurrence. His family history was interesting from the point of view that the patient's father, paternal grandfather and two paternal uncles died of coronary thrombosis between the ages of forty-five and sixty-one. Physical examination revealed a well developed man of healthy appearance, 5 feet, 5 inches tall and weighing 155 pounds, with a blood pressure of 128/66 mm. Hg. There was a grade 1 apical systolic murmur. No other significant findings were noted.

Comment: The etiology of left bundle branch block cannot be ascertained. The presence of scarlet fever in childhood documents the pres-

ence of streptococcal infection and suggests myocarditis as a likely etiology. The strong family history of coronary artery disease, on the other hand, suggests this as an etiologic factor.

Cases 11, 12 and 13 were subjects thirty-eight, thirty-eight and twenty-nine years of age and apparently asymptomatic. They were not available for clinical evaluation.

The electrocardiographic, vectorcardiographic and exercise tests performed on ten subjects evaluated clinically are summarized in Table I. Only one subject demonstrated a QRS pathway that began anteriorly. Only one subject demonstrated S-T segment changes after a double exercise test. The fasting blood sugar, cholesterol and phospholipid studies were within normal limits for the entire group.

SERIES B

This group includes twelve cases of left bundle branch block not found as part of the electrocardiographic survey. They are of importance concerning the etiology of left bundle branch block.

CASE 14. R. B. was a thirty year old officer who consulted a physician for symptoms of fatigue and vague pain in the chest which was non-specific in character. A routine electrocardiogram demonstrated complete left bundle branch block. On subsequent evaluation at the School of Aviation Medicine he appeared to be a healthy young officer who demonstrated a fairly loud systolic murmur of grade 2 intensity over the base of the heart. He continued to complain of symptoms of muscular aching over the shoulders and the interscapular region. Approximately one year after left bundle branch block was noted, extensive stress tests were carried out with treadmill and ventilation studies. These revealed deficiencies in performance as compared to normally healthy persons.

Comment: The presence of pain in the chest and fatigue of the severity described by this officer in association with the left bundle branch block suggests the possibility of myocarditis. Significant coronary artery disease cannot be excluded even in a subject of this age. This officer has been followed up for over two years after detection of left bundle branch block, and no adverse clinical symptoms or findings have been demonstrated.

CASE 15. L. D. was an asymptomatic thirty-one year old officer. His past history included a questionable episode of scarlet fever at age nine without complications. He had bronchial pneumonia at twenty-three years of age. He was rejected from military service in 1943 because of albuminuria, although there was no history of renal disease or subsequent evidence of albuminuria. He weighed 202 pounds at age nineteen. He was then employed as a lumber jack.

A routine electrocardiogram recorded at thirty-one years of age was abnormal (Fig. 3). The abnormality consisted of rudimentary R waves across the anterior precordium with deeply inverted T waves. These findings were strongly suggestive of myocardial infarction of the anterior wall, and it was requested that he be evaluated in consultation. In the interim between recording of the abnormal electrocardiogram and the time of his consultation he had fallen off the back of a truck, sustaining a linear fracture of the occipital skull. He was unconscious for three to four minutes following the fall and shortly thereafter marked lethargy developed although he could be easily aroused. The only residual of the injury to the head was amnesia for the twenty-four hour period following the fall. Subsequent follow-up examination revealed no evidence of neurologic or electroencephalographic defects.

Physical examination revealed a white man of healthy appearance, 5 feet, 11 inches tall, weighing 188 pounds and with a blood pressure of 130/72 mm. Hg. There was a grade 1 systolic murmur heard along the left sternal border and at the apex. There were no other significant physical findings. An electrocardiogram at the time of consultation one year after the first tracing demonstrated complete left bundle branch block.

Comment: This case is extremely interesting because it demonstrates an abnormal electrocardiogram recorded as a routine part of an examination. This electrocardiogram is strongly indicative of a lesion of the anterior wall of the left ventricle. This, in itself, is a reminder that cardiac disease can occur in young people without presenting significant symptoms which are recalled by the patient. The presence of left bundle branch block found one year later is further substantiation that cardiac disease was present. A case such as this clearly demonstrates the fallacy of assuming that the presence of left bundle branch block in the young asymptomatic subject is innocuous. The previous recording one year earlier of an electrocardiogram strongly suggestive of infarction of the anterior wall is beneficial in clarifying the etiology of left bundle branch block in this case. The serial electrocardiograms suggest that a silent myocardial infarction had occurred and one year later was obscured by the development of complete left bundle branch block. In the absence of the

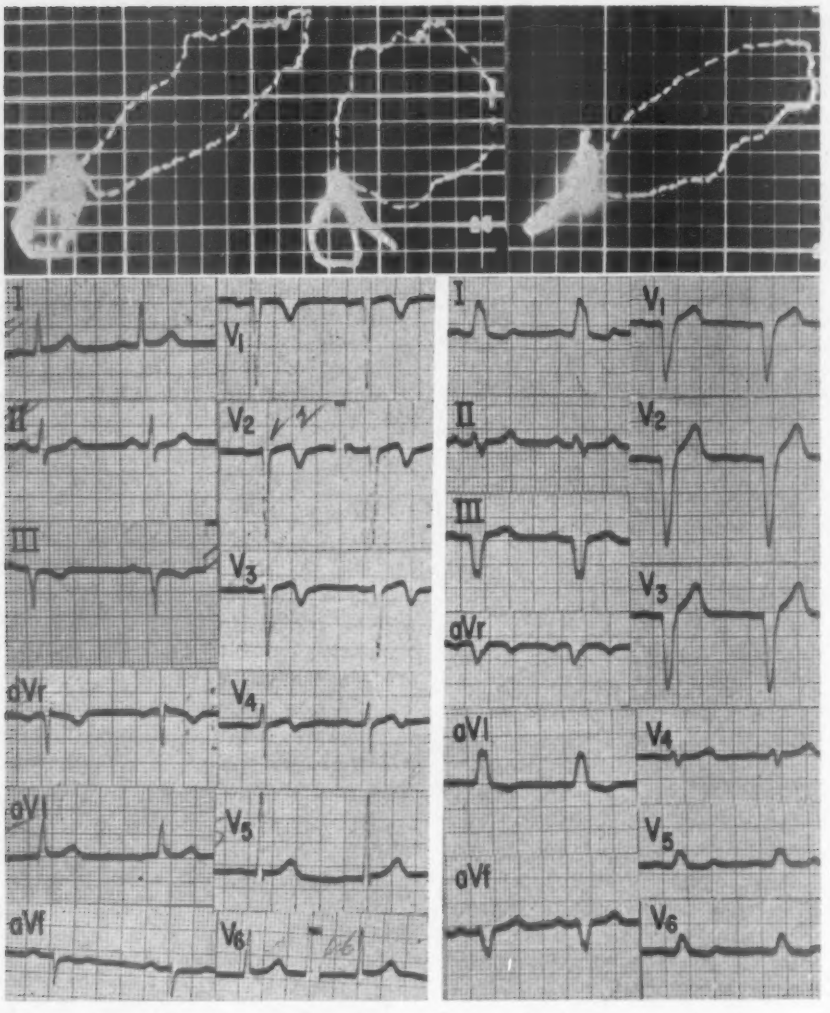


FIG. 3. Case 15. A routine electrocardiogram (*left*) demonstrates abnormal features compatible with disease of the anterior myocardial wall. A subsequent electrocardiogram (*right*) demonstrates complete left bundle branch block. The QRS loop of the vectorcardiogram is counterclockwise in the frontal (*left*) and saggital (*center*) plane and clockwise in the transverse plane (*right*). The T loop is directed opposite the QRS loop.

previous abnormal electrocardiogram, one might have been tempted to assume the erroneous conclusion that left bundle branch block in this subject was without clinical significance.

CASE 16. L. H. sought medical attention for severe coughing spells, audible expiratory wheezing and asthmatic symptoms. An electrocardiogram recorded during the acute illness demonstrated complete left bundle branch block. In 1956 he was hospitalized for diarrhea and weight loss. A bromsulphalein test showed 10 per cent retention after forty-five minutes. He had previously had diarrhea in 1953 while stationed in India. A diagnosis of amebiasis was entertained in view of recurrent episodes of diarrhea, and a course of chloroquine and carbisone was given. Physical examination at the time of his consultation revealed a young, asthenic man weighing 122 pounds. The edge of the liver was palpable one fingerbreadth below the right costal margin. There was no evidence of pulmonary disease. The blood pressure was 120/80 mm. Hg, although on other examinations it was found to be 160/110 mm. Hg and 146/100 mm. Hg. Tests of liver function were normal as were studies of pulmonary function. However, a two-hour postprandial blood sugar test gave a result of 130 mg. per cent. The blood sugar measurements following a glucose tolerance test were as follows: fasting, 100 mg. per cent; one-half hour, 228 mg. per cent; one hour, 217 mg. per cent; two hours, 117 mg. per cent; and three hours, 50 mg. per cent. A diagnosis of mild diabetes mellitus, controlled by diet alone, was made.

Comment: This patient presented himself for respiratory complaints which were sub-

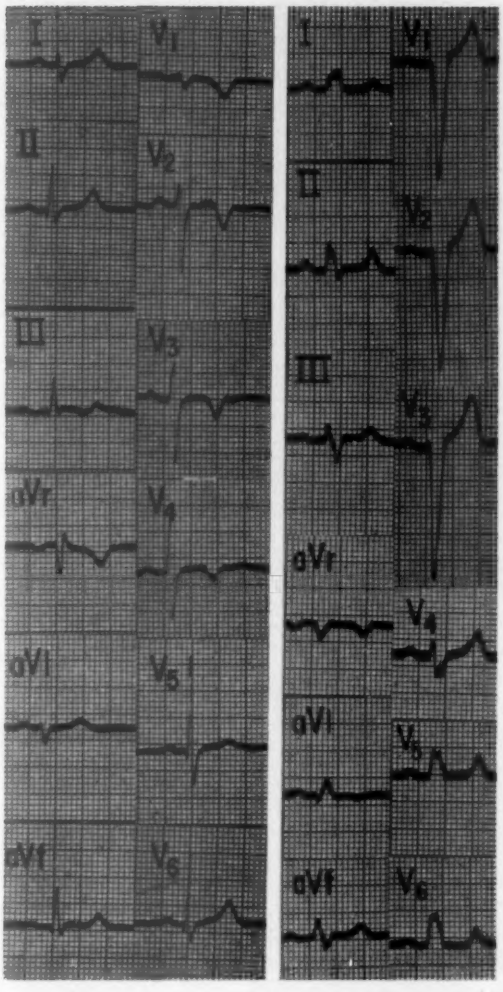


FIG. 4. Case 17. A routine electrocardiogram (*left*) demonstrates T wave inversion in leads V_1 to V_4 which were not present one year earlier. A repeat tracing (*right*) demonstrates development of complete left bundle branch block.

sequently ascertained to be associated with an allergic response of a temporary nature. In the course of the examination he was found to be a vascular hyperreactor and to have diabetes. Vascular disease is a common complication of diabetes. The etiology of the left bundle branch block must remain a matter of opinion. The presence of diabetes and the borderline blood pressure determinations strongly suggest underlying coronary artery disease.

CASE 17. D. P. was a thirty-two year old asymptomatic officer. A normal electrocardiogram was recorded in 1957 as a part of an annual examination. One year later an electrocardiogram demonstrated inversion of the T waves in leads V_1 through V_4. This tracing was originally interpreted as a persistent juvenile pattern. However, since a normal tracing had been previously recorded, the electrocardiogram was repeated in October 1958. At this time left bundle branch block was apparent (Fig. 4). The past history was significant in that he had one episode of pain in the chest in 1955 described as sharp in character and located in the left infrascapular region, aggravated by coughing and deep breathing. Laboratory studies demonstrated a mild leukocytosis which was attributed to pleurisy. He had an urticarial reaction to penicillin in 1952. His family history was interesting in that his father, although aged sixty-two, suffered what was described as a heart attack at age thirty-five. On physical examination the patient gave a healthy appearance, was 6 feet, 1 inch tall and weighed 193 pounds. The blood pressure was 136/86 mm. Hg. There were no other significant physical findings.

Comment: The demonstration of a normal electrocardiogram, followed by an abnormal electrocardiogram consisting of T wave changes across the anterior precordium, and later by development of complete left bundle branch block confirms the presence of relatively recent myocardial disease. The most likely etiology is either myocarditis or coronary artery disease. Either could be expected to produce this sequence of clinical events. In any case, the possibility of an innocuous congenital lesion is adequately excluded.

CASE 18. M. B. was a thirty-six year old officer who was discovered to have complete left bundle branch block at the time of a routine annual physical examination. Two years prior to this examination he had suffered an episode of acute indigestion. His physician recorded an electrocardiogram which was normal. No subsequent electrocardiograms were taken during the acute illness. There were no other significant features to the history. Physical examination revealed a robust young officer, 6 feet, 1 inch tall, weighing 210 pounds. The blood pressure was 145/90 mm. Hg in the right arm and 160/100 mm. Hg in the left arm. There were no other significant physical findings. The blood cholesterol was 358 mg. per cent.

Comment: The presence of a previous normal electrocardiogram in this subject excludes the possibility of long standing left bundle branch block or left bundle branch block of congenital origin. The previous history of indigestion of sufficient severity to prompt his physician to record an electrocardiogram is strong evidence that the episode of indigestion may well have been secondary to cardiac disease. A presumptive diagnosis of coronary artery disease was made.

CASE 19. W. P. was a thirty-eight year old officer who was found to have complete left bundle branch

block at the time of his annual physical examination. The electrocardiogram previously recorded as a part of the electrocardiographic survey was within normal limits. It was learned that approximately sixteen months prior to the detection of complete left bundle branch block he suffered pain in the right anterior part of the neck which radiated into the sternoclavicular region on the right. The pain occurred only with exertion, but was of sufficient severity that the patient would stop and clutch his neck spontaneously. The pain was brief in duration and stopped abruptly after exertion was discontinued. At the time of clinical symptoms the officer had gained appreciable weight and had limited opportunities for physical activity. He also complained of occasional aching pain in the left posterior part of the neck and in the shoulders. This was associated with numbness and tingling radiating into the left forearm. This pain had previously been attributed to a cervical disc with irritation of the nerve root as evidenced by history and the roentgenographic finding of narrowing of interspaces C5 and C6 with a slight reversal of the normal curve of the cervical spine. Physical examination revealed a man of healthy appearance, 6 feet, 2 inches tall and weighing 183 pounds. The blood pressure was 126/88 mm. Hg. There were no other significant findings.

Comment: Although some confusion may have been expected at the initial onset of symptoms in the absence of other supporting data, the history of pain in the neck occurring only with exertion indicates atypical angina. The subsequent development of complete left bundle branch block in the face of a previously normal electrocardiogram is confirmatory evidence of an acute myocardial process. The onset of angina in the absence of valvular or congenital heart disease is suggestive evidence of a small myocardial infarction. This officer had another evaluation eight months after left bundle branch block was discovered. A normal electrocardiogram was obtained which was not significantly different from that obtained prior to the onset of left bundle branch block. Increase in cardiac rate associated with exercise caused left bundle branch block to recur.

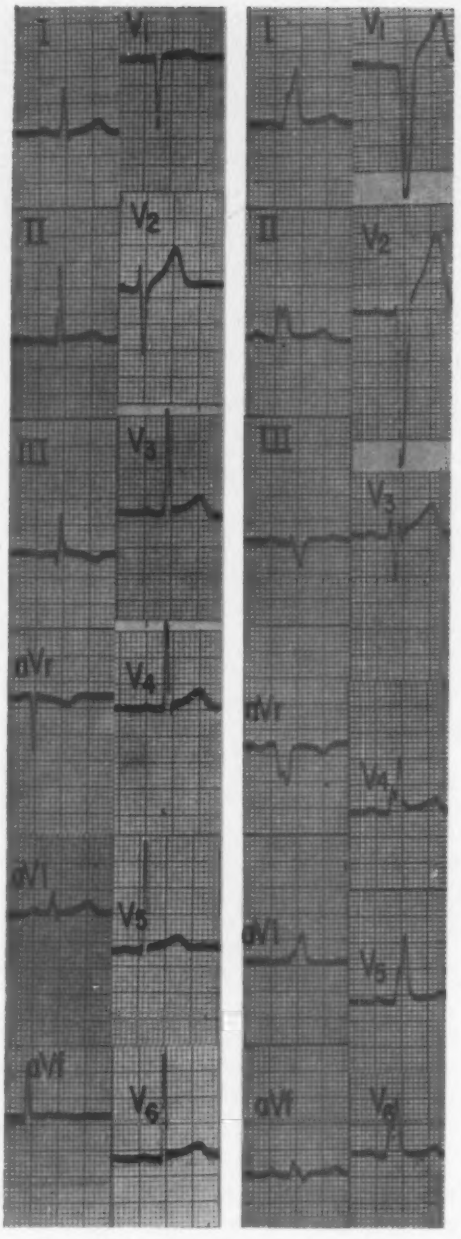


FIG. 5. Case 21. A routine electrocardiogram (*left*) was recorded at the time of annual physical examination. One year later (*right*) left bundle branch block was noted.

CASE 20. B. P. was a forty-one year old asymptomatic officer found to have complete left bundle branch block during a routine electrocardiogram. His past history revealed scarlet fever at two years of age. Physical examination was that of a well developed officer 6 feet tall, weighing 182 pounds. Blood pressure was 130/88 mm. Hg. There were no other significant physical findings. The electrocardiogram was not typical of complete left bundle branch block due to the absence of plateau formations of the QRS complex in lead I. However, the QRS duration was 0.12 second. A previous electrocardiogram was recorded at the time of the annual physical examination one year prior to this particular tracing. It was abnormal in that R waves were absent in leads V_1, V_2 and V_3. Between the time of recording the two electrocardiograms there was a definite increase in the QRS interval.

Comment: The interesting feature in this case is the recording of a previous electrocardiogram strongly suggestive of an infarction of the anterior myocardial wall. The increase in QRS

duration since that time without the clinical development of left ventricular hypertrophy points to a conduction defect. Because of the appearance of the QRS complexes some authorities might choose to call the second record incomplete or atypical left bundle branch block. Nevertheless, the sequence of the electrocardiograms suggests the presence of myocardial disease.

CASE 21. E. P. was a forty-one year old officer who, on a routine electrocardiogram, was found to have complete left bundle branch block. A previous record taken one year earlier, as part of the electrocardiographic survey, was within normal limits (Fig. 5). A subsequent electrocardiogram recorded one month after the record showing complete left bundle branch block was again normal. Prior to the demonstration of the abnormal electrocardiogram the patient complained of episodes of paroxysmal nocturnal dyspnea. These were relieved by taking tranquilizers. The episodes occurred after retiring at night and shortly before falling asleep. They apparently were not associated with emotional or physical stresses. In nearly every instance premonitory expiratory wheezing of mild degree had developed in the early portion of the evening prior to retiring. He complained of the sensation of shortness of breath when approaching an altitude of 9,000 to 10,000 feet in level flight. Shortness of breath was particularly severe when performing any type of physical activity. These sensations were always relieved by the administration of oxygen. He also complained of having experienced several episodes of high epigastric burning after eating a heavy meal during the past year, relieved by alkali. He had never experienced pain in the chest. He had "infectious yellow jaundice" during military service in 1945 and was hospitalized for ten days. Recovery was uneventful. Past history revealed an episode of aching pain of moderate severity of both shoulders and arms, but more pronounced on the left, approximately two years before consultation.

Physical examination revealed a well developed man, 5 feet, 10 inches in height, weighing 178 pounds, with a blood pressure of 138/88 mm. Hg. The retinal arterioles showed minimal A-V nicking. There were no other significant physical findings. An electrocardiogram recorded at the time of his consultation visit was within normal limits. A double exercise test was normal as were tests of pulmonary function. A follow-up evaluation two months later again demonstrated complete left bundle branch block.

Comment: It is difficult to evaluate the clinical history of this subject. No apparent etiology for paroxysmal dyspnea was detected. It is possible that this symptomatology was related to an allergen, rather than cardiovascular disease. The vague discomforts in the chest and indigestion which he described are also difficult to evaluate. The history should be evaluated in the light of subsequent information that this officer was later presented to a physical evaluation board for retirement. It is difficult to state what influence the combination of events of expected removal from flying duty with its loss of pay benefits and subsequent presentation to a physical evaluation board for a disability evaluation has on the patient's symptomatology. Many of these symptoms were documented by his medical records prior to the time the left bundle branch block was noted. Certainly, the finding of a previous normal electrocardiogram in a person with this multiplicity of ill-defined complaints and the subsequent demonstration of left bundle branch block is sufficient evidence to entertain the diagnosis of underlying coronary artery disease. The demonstration of intermittent left bundle branch block is not a rare finding. Most of these patients eventually demonstrated permanent or fixed left bundle branch block; apparently the electrocardiogram in this patient now shows permanent left bundle branch block.

CASE 22. This forty year old asymptomatic officer was found to have complete left bundle branch block at the time of his annual physical examination. The electrocardiogram was recorded prior to the electrocardiographic survey. He had suffered severe thyrotoxicosis in 1948 for which he was hospitalized; a thyroidectomy was performed at that time. The only residual evidence was persistent marked exophthalmos. He had scarlet fever as a child; otherwise the history was non-contributory. Physical examination revealed the presence of prominent exophthalmos persistent for over eight years. There was a slight tremor of both hands and the palmar surface of both hands presented distinct red mottling. The thyroidectomy scar was noted. There were no other significant findings. Extensive laboratory studies were essentially normal. The blood cholesterol was 189 mg. per cent; basal metabolic rate was −10; and the serum protein-bound iodine was 9.1 μg.

Comment: The history of previous thyrotoxicosis and the presence of a high normal protein-bound iodine makes the diagnosis of coronary artery disease less likely. Two etiologies for left bundle branch block are suggested in this case. A possibility of severe thyrotoxicosis having an adverse effect on the myocardium must be considered and the childhood history of scarlet fever suggests the possibility

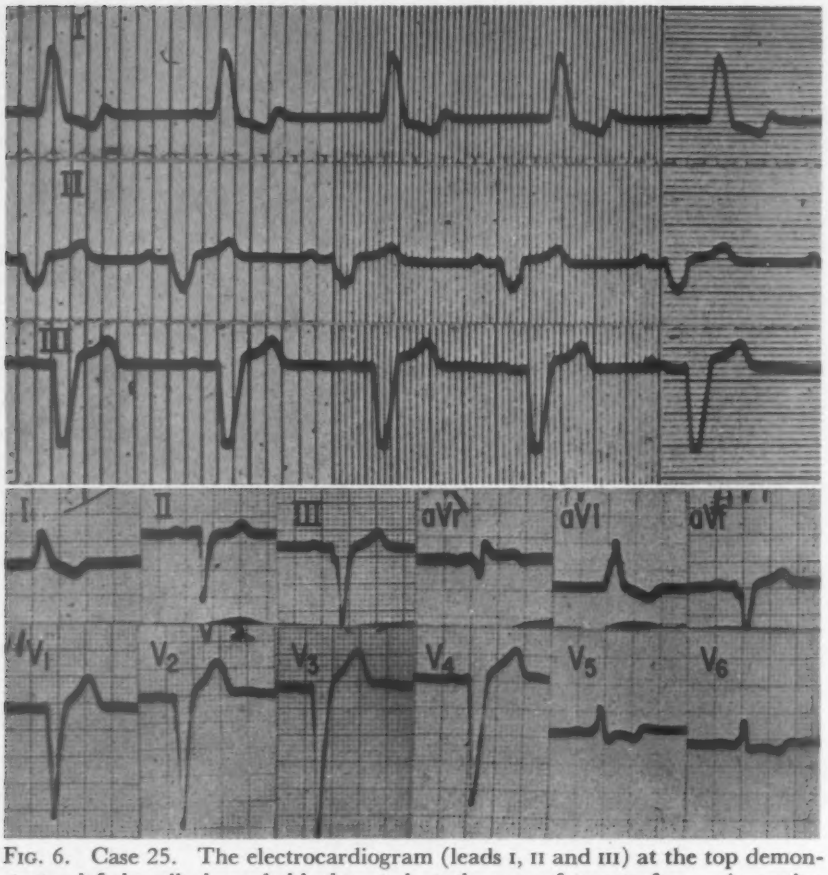


FIG. 6. Case 25. The electrocardiogram (leads I, II and III) at the top demonstrates left bundle branch block noted at the age of twenty-four. A routine electrocardiogram at age forty-six (twenty-two years later) is at bottom.

of rheumatic myocarditis secondary to a streptococcal infection. It is unlikely that left bundle branch block has occurred in this particular subject without some acquired disease in the conduction system.

CASE 23. R. S. was a forty-seven year old officer in apparent good health. At the time of his routine physical examination, an electrocardiogram demonstrated complete left bundle branch block. Because he was past the age of forty, previous electrocardiograms had been recorded; all were within normal limits. Past history was non-contributory and the physical examination revealed no finding other than those consistent with the officer's age.

Comment: Demonstration of annual normal electrocardiograms up to the age of forty-seven and the subsequent development of left bundle block are indicative of a recent acute process and exclude childhood carditis or congenital heart disease as an etiologic factor. The most likely diagnosis is underlying coronary artery disease with degeneration of the left bundle.

CASE 24. G. H. was a fifty-five year old asymptomatic officer whose previous electrocardiograms were normal. At the time of his annual physical examination a routine electrocardiogram demonstrated complete left bundle branch block. Physical examination showed no significant findings other than moderate obesity and changes consistent with his age.

Comment: This is another example of left bundle branch block of recent origin documented by previous recordings of normal electrocardiograms. Its occurrence in a man of this age is evidence of degenerative changes in the myocardium which are most likely secondary to coronary artery disease.

CASE 25. R. J. was a forty-six year old officer. A routine electrocardiogram recorded during all of his annual physical examinations demonstrated complete left bundle branch block. He had had an electrocardiogram of standard leads I, II and III recorded at age twenty-four for purposes of obtaining life insurance (Fig. 6); complete left bundle branch block was demonstrated on that record. The past history is significant only in that scarlet fever had occurred in childhood. Physical examination was unremarkable.

Comment: The documented presence of complete left bundle branch block at age twenty-four

in this officer and the subsequent follow up at the age of forty-six, together with the past history of scarlet fever are strong evidence that left bundle branch block was due to myocarditis, presumably on a rheumatic basis, but the abnormality itself was not sufficient to cause significant impairment of cardiovascular function. As a result, a normal life with usual physical activity was carried on for a period of over twenty-two years without any complications. This is one of the longest follow-up studies of left bundle branch block that have been reported.

Comments

A careful review of the literature fails to give any supporting evidence to the possibility of isolated congenital left bundle branch block. The majority of the cases reported in the literature are in older persons. Many of these, for whom case reports are available, demonstrate adequate causes for the development of left bundle branch block. These include such factors as hypertension or discovery of the lesion in an age group in which coronary artery disease is a common finding. Reports of young people with complete left bundle branch block are often associated with a documented history of acute myocardial infarction. The simple follow-up evaluation for a period of seven to twelve years after discovery of left bundle branch block is not sufficient evidence to indicate that left bundle branch block is present without significant disease. The follow-up evaluation of patients with documented myocardial infarctions for periods of ten to twenty years is not unknown to medical literature. Such follow-up studies, however, do not indicate that myocardial infarction is an innocuous finding.

This large electrocardiographic survey (series A) points up the rarity of complete left bundle branch block in a healthy population. The incidence of left bundle branch block was only 0.9 per 10,000 below the age of thirty-five and 4 per 10,000 above the age of thirty-five years. This is a sharp contrast to the incidence of complete right bundle branch block. Moreover, an evaluation of ten of the subjects found in the routine survey demonstrated a high degree of clinical illnesses or findings suggestive of cardiac involvement, and certainly capable of producing complete left bundle branch block. The associated findings included previous rheumatic fever, previous acute nephritis, vascular hyperreactivity, previous streptococcal infection of the throat requiring hospitalization, associated leiomyoma of the esophagus, previous diphtheria, previous childhood pneumonia and the possibility of underlying arteriosclerotic heart disease, previous labyrinthitis and previous scarlet fever in a patient with a strong family history of coronary artery disease. None of these cases lend much support to the concept that left bundle branch block can exist as an isolated abnormality. In the majority of the ten cases of complete left bundle branch block found in series A, the previous history or evidence of illnesses commonly associated with heart disease was brought to light when electrocardiograms demonstrated the presence of complete left bundle branch block.

Series B presents a number of unusual features. The presence of previous normal baseline records in many of the subjects adequately excludes the possibility of congenital origin of complete left bundle branch block. The demonstration of previous abnormality on the routine electrocardiogram permitted positive diagnosis in certain instances. One of the most striking of these was the demonstration of an electrocardiogram presenting strong evidence of previous disease of the anterior wall of the left ventricle, even though the subject was a young, asymptomatic officer, illustrating the relative innocuousness of residual cardiac disease in some instances. One patient in this series (Case 25) demonstrates the long term follow up of innocuous left bundle branch block.

Clinical Significance and Prognosis: These studies support the concept that left bundle branch block is evidence of underlying cardiac disease, and not an isolated defect in the left bundle on a congenital basis. The important question to decide when left bundle branch block is found is not whether or not disease is present, but how significant it might be. In well documented cases of previous scarlet fever or diphtheria the probability of underlying myocarditis as the etiologic factor should receive first consideration. The high incidence of coronary artery disease even in the young age group requires that arteriosclerotic disease be considered as a major cause for the occurrence of left bundle branch block, and even the presence of childhood scarlet fever does not permit positive exclusion of atherosclerosis without previous electrocardiograms. The relatively low incidence of left bundle branch block as compared to right bundle branch block, and the relatively high

incidence of associated cardiac disease substantiate the point of view that the prognosis in the presence of left bundle branch block is not as good as in right bundle branch block. Whereas the prognosis for right and left bundle branch block may be considered equal if both are associated with underlying coronary artery disease, it is obvious that considerable difference exists between the patient who presents with left bundle branch block due to coronary artery disease and the patient with complete right bundle branch block due to an isolated congenital finding. Previous reports in the literature have not taken credence of the comparative differences in incidence of left and right bundle branch block in the asymptomatic population. Almost all studies are drawn from hospital and clinical data in which the majority of the patients seeking medical consultation present with definite heart disease of such a nature as to require medical consultation.

These comments are not meant to indicate that the prognosis in left bundle branch block is necessarily poor. The patient with left bundle branch block secondary to mild myocarditis during his childhood, has a good opportunity to lead a normal and unrestricted life. The major importance in recognizing that left bundle branch block is primary evidence of underlying cardiac disease is in those few instances in which insurability must be ascertained, or when the patient wants to participate in activities or occupations which present a hazard to the cardiovascular system. The inability to exclude in a rather positive manner significant organic heart disease in the rare patient presenting with left bundle branch block is sufficient evidence to require some degree of clinical caution before indiscriminately advising such a patient to engage in occupations which expose him to hypoxia or to any other forms of unusual or exceptional stress on the cardiovascular system. In order that this opinion may not be misconstrued, it should be emphasized that in the absence of other findings, these people can lead normal lives with normal physical activity, but reasonable caution should be exercised before advising the unusual.

Summary

As a result of routine electrocardiograms taken on 67,375 apparently healthy subjects from the U. S. Air Force flying population, only thirteen examples of complete left bundle branch block were found. The majority of the thirteen subjects had a significant past history that suggested an acquired defect of the heart. This study points up the fact that complete left bundle branch block in a healthy population is a rare finding (1 in 5,000).

Complete left bundle branch block was found in twelve other men during examination for other reasons. They are not included in the statistics of the survey but they do present important evidence concerning the etiology of asymptomatic left bundle branch block.

This study presents evidence that left bundle branch block is the result of cardiac disease and is evidence of cardiac disease. In certain instances the cardiac involvement may be minimal, creating no major adverse effects.

References

1. Rosenman, R. H., Pick, A. and Katz, L. N. Intraventricular block—review of the literature. *Arch Int. Med.*, 86: 196, 1950.
2. Yater, W. M. Pathogenesis of bundle branch block. *Arch. Int. Med.*, 62: 1, 1938.
3. Graybiel, A. and Sprague, H. B. Bundle branch block: an analysis of 395 cases. *Am. J. M. Sc.*, 185: 395, 1933.
4. Langley, R. W., Reed, J. C. and Utz, D. C. Bundle branch block: a review of 100 cases. *Am. Heart J.*, 33: 730, 1947.
5. Lamb, L. E., Averill, K. H. and Dermksian, G. Intermittent right bundle branch block without apparent heart disease. *Am. J. Cardiol.*, 4: 302, 1959.
6. Wolfram, J. Bundle branch block without significant heart disease. *Am. Heart J.*, 41: 656, 1951.
7. Vazifdar, J. P. and Levine, S. A. Benign bundle branch block. *Arch. Int. Med.*, 89: 568, 1952.
8. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew. *Circulation*, 10: 384, 1954.
9. Packard, J. M., Graettinger, J. S. and Graybiel, A. Analysis of the electrocardiograms obtained from 1000 young, healthy aviators: ten year follow-up. *Circulation*, 10: 384, 1954.
10. Kremer, R. and Delchevalerie, J. Cardiomegalie familiale avec blocs de branche. *Acta cardiol.*, 12: 527, 1957.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

VI. Right Bundle Branch Block*

MAJ. ROBERT L. JOHNSON, MC, USAF, CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THIS report is an analysis of 106 cases of complete right bundle branch block found in an electrocardiographic survey of 67,375 apparently healthy, asymptomatic adults. The survey provided a unique opportunity to study right bundle branch in a population assumed to be disease-free. The majority of previous studies of right bundle branch block are from clinic and hospital series of symptomatic patients, most often presenting with heart disease. Although a number of surveys of normal subjects have been accomplished, the low incidence of complete right bundle branch block (0.16 per cent) necessitates a large survey to obtain very many examples.[1–4] The age distribution of the population in the present study (sixteen to sixty-three years) permits an analysis of the frequency of this abnormality in different age groups. Only cases of complete right bundle branch block with a QRS duration of 0.12 second or over and a broad S wave in lead I associated with a broad terminal R′ wave in lead V_1 are included.

MATERIAL AND METHODS

Each example of right bundle branch block in this survey was discovered by a routine electrocardiogram obtained to fulfill examination requirements for flying. The details of the survey have been outlined elsewhere.[5] In twenty-seven instances the subject was studied in detail at the School of Aviation Medicine. Each subject had a thorough medical and roentgenographic examination, and routine laboratory studies, including, in most instances, blood cholesterol, phospholipids and fasting blood sugar determinations. Special electrocardiographic procedures included the Master exercise test and records obtained under orthostatic influences, during breath-holding, hyperventilation, oxygen breathing, controlled positive pressure breathing, carotid sinus massage and following injection of atropine. Spatial vectorcardiograms were obtained using the electrically balanced bipolar vectorcardiographic reference system.[6–8]

Another group of seventeen subjects who were evaluated at their home base had a majority of the aforementioned procedures except vectorcardiography and exercise tolerance tests. In most of the electrocardiograms on the remaining sixty-two subjects the height, weight, blood pressure and age were given.

These data and laboratory studies were tabulated. The characteristics of the electrocardiograms, including intervals, mean QRS axis, initial 0.08 second QRS axis, terminal 0.04 second QRS axis, mean T axis, spatial QRS-T angle, 0.08 second QRS-T angle and the presence of R′ waves in the V leads, were studied. The spatial angles were calculated by means of a chart.[9] All special studies were evaluated for frequency of possibly significant findings.

RESULTS

Age: The frequency of right bundle branch block was fairly constant until the age of forty. Above this age the incidence was increased. This is reflected in comparing a curve of the percentage of subjects in the survey in each five-year age group with the percentage of total number of subjects with right bundle branch block in each five-year age group (Fig. 1). It is also expressed by a graph of the rate per thousand of this abnormality for each five-year age group (Fig. 2). The average rate per thousand between twenty and forty years of age was 1.5 and above forty years of age it was

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

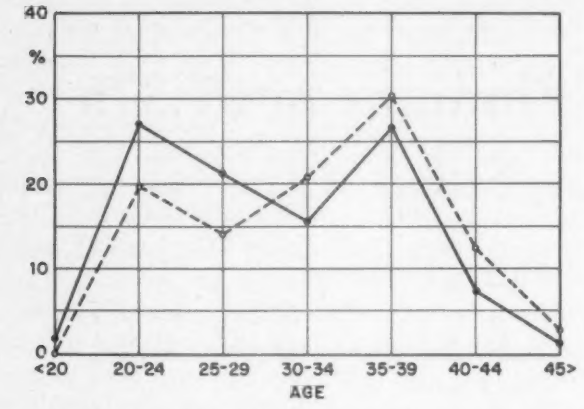


FIG. 1. The solid line demonstrates the per cent of the population surveyed in each five-year age group. The broken line depicts the per cent of all subjects with right bundle branch block in each five-year age group. Comparison of the curves indicates an increase in the incidence of right bundle branch block above the age of thirty.

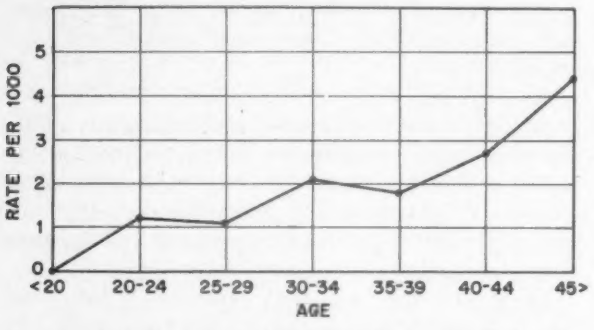


FIG. 2. The rate per thousand depicts a trend of an increased incidence of right bundle branch block with increased age.

TABLE I

Age of 106 Subjects with Right Bundle Branch Block

Age (yr.)	No. of Subjects
20–24	21
25–29	15
30–34	22
35–39	32
40–44	13
Over 45	3

TABLE II

Weight of 105 Subjects with Right Bundle Branch Block

Weight	No. of Subjects
135–144	9
145–154	11
155–164	21
165–174	21
175–184	19
185–194	11
195–204	7
205–214	3
215–224	1
Over 225	2

TABLE III

Mean Weight for Each Five-Year Age Group in 105 Subjects with Right Bundle Branch Block

Age (yr.)	No. in Group	Mean Weight (lb.)
20–24	20	168.5
25–29	16	174
30–34	21	166
35–39	43	171.9
40–44	4	177
Over 45	1	190

TABLE IV

Heart Rate in 106 Subjects with Right Bundle Branch Block

Heart Rate (per min.)	No. of Subjects
50–54	2
55–59	9
60–64	23
65–69	11
70–74	20
75–79	15
80–84	9
85–89	6
90–94	7
95–99	4

2.9. The number of subjects with right bundle branch block in each five-year age group is shown in Table I.

Height and Weight: These measurements were known in 105 subjects. The mean weight was 170.7 pounds; the mode was 160 pounds, representing the weight of twelve subjects. The median weight was 170 pounds. The number of subjects in each weight group is shown in Table II. The mean weight for the subjects in each five-year age group is noted in Table III. No significant difference in weight as related to age was noted in these subjects and as a group they presented no evidence of a greater frequency of increased body weight than other subjects in the survey. Obesity

TABLE V
Blood Pressure in 103 Subjects with Right Bundle Branch Block

Pressure (mm. Hg)	No. of Subjects
Systolic	
91–100	1
101–110	14
111–120	30
121–130	35
131–140	21
141–150	1
151–160	1
Diastolic	
51– 60	4
61– 70	20
71– 80	42
81– 90	35
91–100	1
101–110	1

TABLE VI
Serum Cholesterol Values in Fifty-Two Subjects with Right Bundle Branch Block

Cholesterol (mg. %)	No. of Subjects
126–150	1
151–175	1
176–200	6
201–225	3
226–250	10
251–275	10
276–300	12
301–325	4
326–350	2
351–375	1
376–400	1
401–425	1

TABLE VII
Mean Serum Cholesterol Levels for Each Five-Year Age Group in Fifty-Two Subjects with Right Bundle Branch Block

Age (yr.)	No. in Group	Mean Cholesterol (mg. %)
20–24	3	224
25–29	6	244
30–34	12	246
35–39	29	280
40–44	2	204

did not seem to increase in the group with right bundle branch block. The height ranged from 65 to 77 inches with a median of 70 inches and a mean of 73 inches. The mode for height was 70 inches, representing the height of twenty-seven subjects.

Heart Rate: The heart rate was determined from the electrocardiogram in all subjects. The rate varied from 50 to 98 per minute with a mean of 72 and a median of 70 beats per minute. The distribution of the heart rates is seen in Table IV.

Blood Pressure: The blood pressure was known in 103 subjects. The highest blood pressure was 156/106 mm. Hg. The lowest systolic pressure was noted in a subject whose pressure was 100/70 mm. Hg and the lowest diastolic pressure was noted in a subject whose pressure was 128/58 mm. Hg.

For the group, the systolic pressure had a mean of 123, a median of 122, and a mode (twelve subjects) of 120 mm. Hg. The diastolic pressure was represented by a mean of 78, a median of 80, and a mode (seventeen subjects) of 80 mm. Hg. The distribution of blood pressure is shown in Table V.

Cholesterol and Phospholipid Levels: The serum cholesterol values were known in fifty-two subjects. The range was between 130 and 406 mg. per cent. The mean cholesterol level was 262 and the median was 265. The mode representing twelve subjects was 276 to 300. The cholesterol levels are shown in Table VI. The mean cholesterol level for each five-year age group is depicted in Table VII. Between

TABLE VIII
Serum Phospholipid Values in Forty-One Subjects with Right Bundle Branch Block

Phospholipids (mg. %)	No. of Subjects
126–150	1
151–175	1
176–200	3
201–225	3
226–250	12
251–275	4
276–300	9
301–325	3
326–350	3
351–375	1
376–400	0
401–425	0
over 425	1

TABLE IX
Mean Phospholipid Levels for Each Five-Year Age Group in Forty-One Subjects with Right Bundle Branch Block

Age (yr.)	No. in Group	Mean Phospholipid (mg. %)
20–24	3	223
25–29	4	203
30–34	10	277
35–39	23	278
40–44	1	275

TABLE X
Duration of QRS Complexes in 106 Subjects with Right Bundle Branch Block

QRS Duration	No. of Subjects	Per Cent of Subjects
0.12	14	13.2
0.13	25	23.6
0.14	41	38.7
0.15	16	15.1
0.16	10	9.4

TABLE XI
Presence of R′ Waves in V Leads of 106 Subjects with Right Bundle Branch Block

R′ Present in	No. of Subjects
V_1 only	74
V_1 and V_2	24
V_1 to V_3	6
V_1 to V_4	2

TABLE XII
Q-T Interval in 106 Subjects with Right Bundle Branch Block

Q-T Interval (sec.)	No. of Subjects
0.34	3
0.35	2
0.36	8
0.37	4
0.38	11
0.39	11
0.40	29
0.41	13
0.42	9
0.43	6
0.44	7
0.45	2
0.46	1

the ages of thirty-five and thirty-nine years the mean cholesterol level was 280, representing an increase above the levels noted below the age of thirty-five years. The phospholipid level varied between 135 and 374 mg. per cent. The mean value was 266 and the median 250. The mode representing twelve subjects was between 226 and 250. The values for the phospholipid levels are seen in Tables VIII and IX.

QRS Complex: The QRS duration was 0.12 second or greater in all subjects. The longest QRS duration in any lead was used for the interval. A broad S wave in lead I and a broad terminal R′ wave in lead V_1 of greater amplitude than the initial R wave were present in all. The longest QRS interval was 0.16 second, noted in ten subjects. The number of subjects with different QRS durations is noted in Table X. The presence of a large R′ wave in lead V_1 but not in leads V_2 to V_6 was noted in seventy-four subjects. The presence of an R′ wave in different V leads for the 106 subjects is given in Table XI.

Q-T Interval: The Q-T interval varied between 0.34 and 0.46 second. The frequency of different Q-T intervals is shown in Table XII.

T Vector: The axis of the T wave in the frontal plane was between −15 and +75 degrees. The frequency of different T axes is noted in Table XIII. The T wave was normal in all instances.

QRS Axis: The mean QRS axis was determined for all records. This determination is limited in accuracy since the diphasic characteristic of the QRS complexes in the limb leads results in an axis that is nearly indeterminate. Since the major alteration of the QRS complex in right bundle branch block frequently appeared to be restricted to the terminal portion

TABLE XIII
T Axis in the Frontal Plane in 106 Subjects with Right Bundle Branch Block

Axis (degrees)	No. of Subjects
−15	2
0	13
+15	38
+30	19
+45	27
+60	5
+75	2

of the QRS complex, the initial 0.08 second QRS axis was determined. The latter was more often within the limits of normal. The difference between the mean QRS axis and the initial 0.08 second QRS axis is seen in Table XIV.

QRS-T Angle: The spatial angle between the mean QRS and T vectors was over 60 degrees in seventy-three subjects. The angle between the initial 0.08 second QRS vector and the T vector was greater than 60 degrees in thirty-two subjects. The spatial QRS-T angles are noted in Table XV. The widening of the spatial QRS-T angle in all instances was dependent upon QRS changes, since the T vector was normal in all subjects.

QRS Amplitude: The QRS amplitude was measured by two methods, the sum of leads I, aVF and V_2 and the sum of leads I and aVF. The former method provides a sum of amplitudes along X, Y and Z coordinates and the latter provides a value for the frontal plane only. The range of amplitude is given in Table XVI. Amplitude in right bundle branch block did not appear to be significantly different from the values in the normal population.

TABLE XIV

QRS Axis in the Frontal Plane in 106 Subjects with Right Bundle Branch Block

Axis (degrees)	No. of Subjects	
	Mean QRS Axis	Initial 0.08 sec. QRS Axis
0	4	7
+ 15	1	4
+ 30	2	8
+ 45	3	9
+ 60	6	15
+ 75	5	23
+ 90	0	0
+105	26	16
+120	5	1
+135	12	2
+150	3	3
+165	6	0
180	2	1
−165	3	0
−150	2	0
−135	4	0
−120	4	0
−105	2	0
− 90	0	0
− 75	8	3
− 60	0	3
− 45	2	3
− 30	3	5
− 15	3	3

TABLE XV

Spatial Angles in 106 Subjects with Right Bundle Branch Block

Angle (degrees)	No. of Subjects	
	Angle Between Mean QRS Vector and the T Vector	Angle Between Initial 0.08 sec. QRS Vector and Mean T Vector
0– 10	0	6
11– 20	9	12
21– 30	4	17
31– 40	4	7
41– 50	5	20
51– 60	11	12
61– 70	4	7
71– 80	10	6
81– 90	13	11
91–100	4	1
101–110	7	4
111–120	11	1
121–130	3	0
131–140	7	2
141–150	7	0
151–160	4	0
161–170	2	0
171–180	1	0

TABLE XVI

QRS Amplitude in 104 Subjects with Right Bundle Branch Block

Amplitude (mv.)	No. of Subjects with Amplitude in Leads:	
	I plus aVF plus V_2	I plus aVF
0.7, 0.8	0	3
0.9, 1.0	0	2
1.1, 1.2	1	8
1.3, 1.4	1	13
1.5, 1.6	0	21
1.7, 1.8	2	18
1.9, 2.0	6	14
2.1, 2.2	9	10
2.3, 2.4	9	11
2.5, 2.6	18	1
2.7, 2.8	13	2
2.9, 3.0	5	1
3.1, 3.2	9	0
3.3, 3.4	8	0
3.5, 3.6	9	0
3.7, 3.8	5	0
3.9, 4.0	2	0
4.1, 4.2	2	0
4.3, 4.4	3	0
4.5, 4.6	0	0
4.7, 4.8	1	0
4.9, 5.0	0	0
5.1, 5.2	1	0

TABLE XVII
Double Master Exercise Tests in Twenty-Seven Subjects with Right Bundle Branch Block

Interpretation of Test	No. of Subjects
Normal	25
Borderline	0
Abnormal	2

Double Master Exercise Test: Since most of the subjects in the group did not appear to have heart disease, an excellent opportunity was present to evaluate the electrocardiographic response to exercise in uncomplicated right bundle branch block. This procedure was not carried out for diagnostic purposes since the presence of an abnormal resting tracing does not permit electrocardiographic interpretation after exercise. Of twenty-seven subjects tested only two had an apparent positive response; the rest had no significant changes in the S-T segment (Table XVII). To make an interpretation of a positive test it was required that the S-T segment be depressed in a plateau fashion 1 mm. or more in any lead for two minutes after completing standardized exercise.

Associated Clinical Findings: Complete clinical evaluations were available in forty-four subjects. Of these five subjects had a past history of scarlet fever, one of rheumatic fever and two of diphtheria. Only one admitted having a previous episode of syncope. Apical systolic murmurs thought to be physiologic and of grade 1 or 2 intensity were noted in five subjects. A physiologic systolic murmur at the base was noted in another. One subject had evidence of an atrial septal defect with right heart enlargement, prominent pulmonary artery and a grade 3 systolic ejection murmur at the base of the heart. In two subjects labile elevated blood pressure was found and they were classified as vascular hyperreactors. One subject had gout and another had bronchitis. First degree A-V block was an associated feature in one subject. The remainder of the clinical findings were unremarkable.

COMMENTS

Medical opinion concerning the significance of right bundle branch block has changed markedly since this abnormality was first recognized. Eppinger and Rothberger referred to what is now called left bundle branch block as the common type of bundle branch block. Right bundle branch block was considered uncommon. Previous medical literature on bundle branch block is well summarized by Rosenman, Pick and Katz[10] as well as by Yater.[11] Graybiel and Sprague[12] reported that the average duration of life in 223 fatal cases was one year and two months. It was their opinion that bundle branch block was invariably a manifestation of serious organic heart disease and that partial bundle branch block was equally significant.

In subsequent studies[13-15] conclusions concerning prognosis were derived from a preselected population coming to a medical facility with severe heart disease and in no way reflected prognosis in right bundle branch block in the asymptomatic population. Several authors[16-18] have reported cases of right bundle branch block without evidence of heart disease.

Our series indicates that below the age of forty, right bundle branch block occurs 1.5 times in 1,000 persons and that it is eight times as frequent as left bundle branch block. There appears to be a definite increase in incidence past the age of forty in the male population. Even though the numbers are small, they are undoubtedly significant since most subjects found to have right bundle branch block at the age of forty were removed from flying at the time of previous annual physical examination for that age group. Thus, the age group over forty years was preselected in the sense that many subjects with questionable findings had been removed from the flying population. The most significant finding, however, was the fairly consistent incidence of right bundle branch block below the age of forty for all age groups.

Neither height, weight nor obesity seemed to be a major factor in the frequency of complete right bundle branch block. Blood cholesterol and phospholipid values were not significantly different from values frequently noted in a similar population of American men without clinical evidence of heart disease. Elevated blood pressure was infrequent, as would be expected in such a selected population.

The incidence of associated clinical findings was unremarkable. The single case of atrial septal defect indicates a low incidence of associated congenital abnormalities.

It was of interest to note that the T waves were normal in all subjects. This suggests that the T waves do not change in the presence of uncomplicated right bundle branch block. Significant alteration of T waves in right bundle

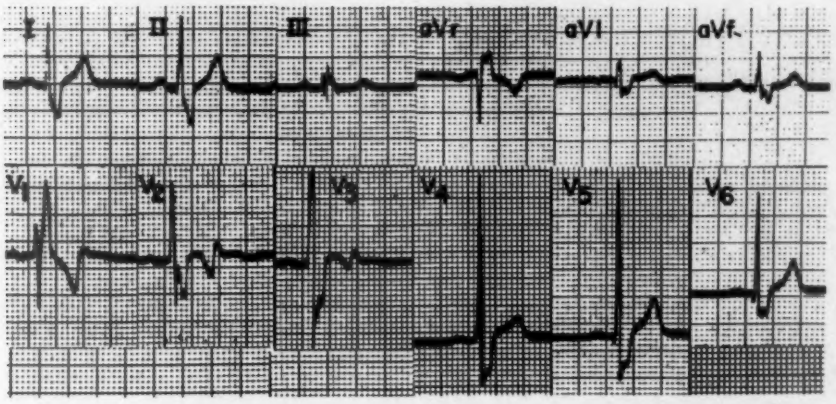


FIG. 3. Complete right bundle branch block with no R′ wave in lead V_2.

branch block should have the same significance as those occurring in subjects with normal QRS complexes.

The frequent normality of the initial 0.08 second interval of the QRS complex implies that the initial events of ventricular excitation are not significantly altered. Comments on this point in the presence of intermittent right bundle branch block may be found in a previous report.[19]

The terminal vector in the presence of complete right bundle branch block is primarily directed to the right and very frequently a true anterior orientation of the vector does not exist (Fig. 3). This is evidenced by the frequency of an R′ wave in lead V_1 and the absence of a significant R′ wave in lead V_2. Lead V_1 is influenced by forces which are directed to the right whether or not they are anterior in orientation. The points mentioned suggest that complete right bundle branch block is not associated with significant alteration in the order of excitation across the main portion of the ventricular septum. It is possible that the abnormality in conduction involves areas of muscle chiefly at the base of the septum or the base of the heart. It is well known that these particular areas are usually poorly supplied by Purkinje fibers of the specialized conducting system. The base of the heart is the last portion of the ventricular muscle mass to complete excitation and, therefore, remains in a relatively refractory period longer than other muscular regions. Conduction through any muscular area which is in the relative refractory phrase is slowed, as commonly seen in aberrant conduction in premature contractions. In addition, the relatively poor distribution of specialized conductive tissue in the base of the heart and base of the septum makes it more likely that a conduction defect in this area would be manifested in subjects without overt heart disease in contradistinction to conduction defects in other regions of the heart muscle as seen, for example, in left bundle branch block.

The exercise tolerance tests carried out in this survey were performed primarily for collection of data. None was interpreted on a clinical basis. Nevertheless, it is interesting that only two subjects showed significant S-T segment depression of 1 mm. or more for two minutes after exercise. The apparent normality of the S-T segment in the majority of the subjects gives some hope that the exercise tolerance test might be of diagnostic value even in the presence of complete right bundle branch block. Follow-up evaluation of the subjects in this study should provide an answer to this point.

Incomplete Right Bundle Branch Block: One of the interesting features resulting from this survey was the documentation of the origin of incomplete right bundle branch block. Since electrocardiograms in this survey were recorded by a variety of technicians throughout the world and frequently interpreted at base level by physicians trained at numerous different medical centers, a cross section of the usual interpretations given was obtained. The most common cause for incomplete right bundle branch block was an incorrectly taken electrocardiogram. Electrodes are frequently placed in the third intercostal space on the chest rather than the fourth for recording of leads V_1 and V_2. In many subjects demonstrating a terminal vector force directed upward toward the right shoulder, if the electrode is placed too high on the chest, an R′ wave will be recorded in the V leads (Fig. 4). This is simply explained by a positive force being directed toward a positive pole. When the precordial electrodes are properly

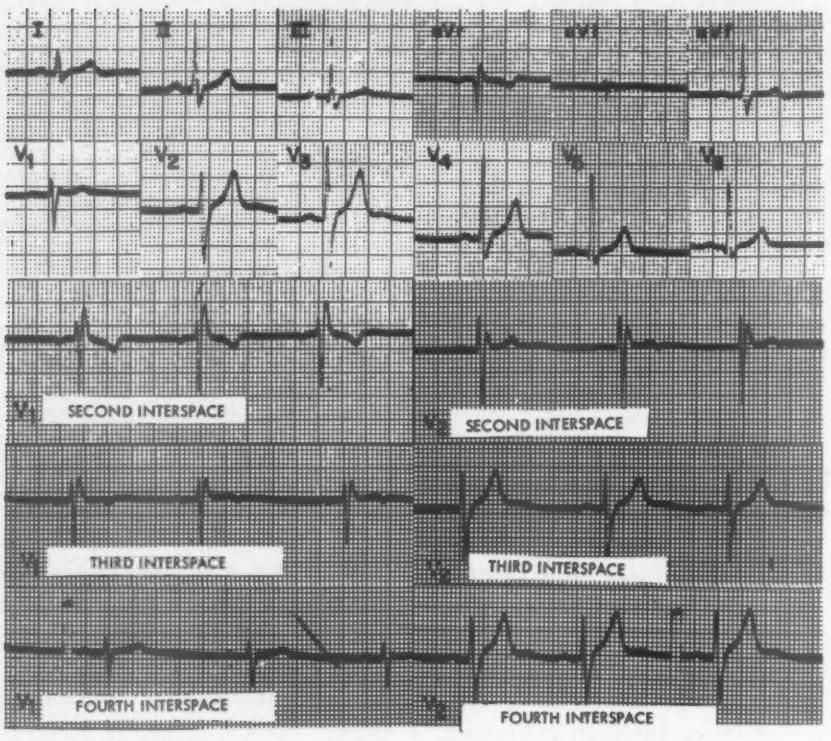


FIG. 4. The routine electrocardiogram (*upper*) demonstrates an $S_1S_2S_3$ pattern with a small r′ wave in lead V_1 and no r′ wave in lead V_2. When the electrodes are placed above their proper position R′ waves and change in P wave configuration are noted.

placed in the fourth intercostal space they are relatively perpendicular to forces directed upward toward the right shoulder that are principally confined to the frontal plane. Such recordings do not demonstrate the presence of significant R′ waves in lead V_1. Failure to appreciate this as a common cause for an R′ wave in lead V_1 causes erroneous interpretation and suggests that the statistics concerning the significance of incomplete right bundle branch block deserve critical analysis.

Even when the electrode is placed in the proper interspace there are some persons with a relatively long thorax in whom the relationship of the heart to the precordial electrodes is distorted. Then the heart is below the usual level of the precordial electrodes, and forces which are directed upward result in positive waves. During inspiration the diaphragm descends and the heart moves below its usual anatomic position. In these circumstances a terminal force directed toward the right shoulder commonly produces an R′ wave at the lead V_1 position (Fig. 5). Precordial maps have proved to be of definite value in evaluating questionable electrocardiograms and careful scrutiny of the roentgenogram of the chest to ascertain the cardiac position in relationship to the intercostal spaces is of value in differentiating electrical artifact from a true conduction defect.

Vectorcardiograms: These were recorded in twenty-seven subjects. In each instance the configuration of the QRS complex in the electrocardiogram could be correlated with the characteristics of the QRS loop. The principal feature of the vectorcardiogram was the slow terminal portion of the QRS loop, directed to the right. Frequently, the initial 0.08 second portion was entirely normal; in other instances the entire QRS loop demonstrated a change in orientation of the electrical field (Figs. 6 and 7). The vectorcardiogram did not provide any information that could not be gained from the twelve-lead electrocardiogram. This does not imply that the vectorcardiogram is not useful, merely that the customary parameters of the vectorcardiogram studied at the present time were not of additional value in these cases. Analyses based on the length of the spatial QRS loop and similar data are meaningless until adequate normal subjects have been studied for comparison.

The demonstration of relatively normal initial QRS loops in the vectorcardiograms

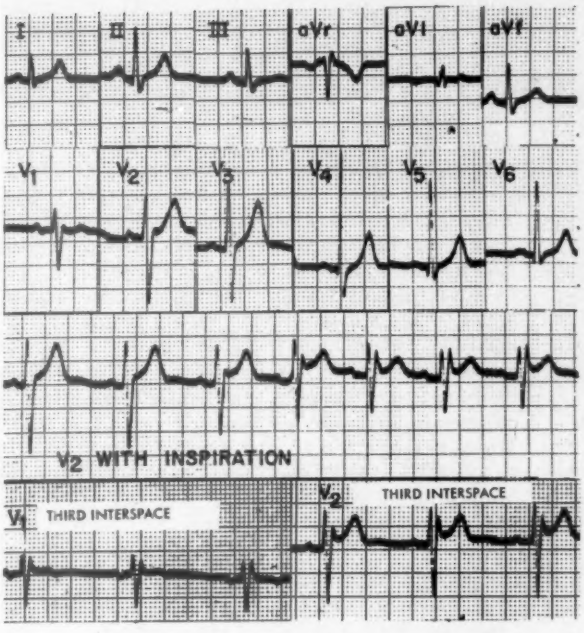


FIG. 5. A routine electrocardiogram demonstrates an $S_1S_2S_3$ pattern. Either inspiration or placing the electrodes too high creates a prominent R′ wave.

FIG. 6. Vectorcardiogram in complete right bundle branch block demonstrating terminal slowing of the QRS loop. In this example the loop is displaced upward. The frontal (*upper left*), sagittal (*upper right*) and transverse (*lower*) planes are shown.

strongly suggests that in many cases of complete right bundle branch block the initial events of ventricular excitation are not altered.

In the presence of apparent right bundle branch block due to unusual relation of the precordial electrode to the heart (misplacement or body configuration), the vectorcardiogram was normal or merely demonstrated the

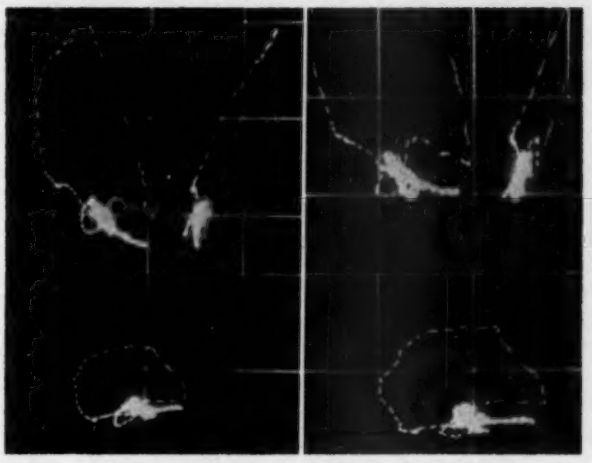


FIG. 7. Vectorcardiogram in right bundle branch block demonstrating deformity of the entire QRS loop. The frontal (*upper left*), sagittal (*upper right*) and transverse (*lower*) planes are shown. The right set was recorded at increased sensitivity.

features of an $S_1S_2S_3$ type of ventricular excitation, without a significant anterior component.

SUMMARY

Complete right bundle branch block was noted in 106 subjects in a survey of 67,375 apparently healthy men. The rate per thousand below the age of forty was 1.5 contrasted to a rate of 2.9 per thousand past the age of forty.

Complete right bundle branch block could not be correlated with an increase in clinical factors thought to be associated with an increased incidence of coronary artery disease. The body weight, blood cholesterol and phospolipid levels and blood pressure were similar in the normal group as compared to the subjects with complete right bundle branch block.

The initial 0.08 second QRS vector was more often normally oriented even in the presence of complete right bundle branch block, suggesting that the initial events of ventricular excitation are relatively unaltered in the presence of uncomplicated right bundle branch block.

The T waves were normal in all, suggesting that the presence of right bundle branch block does not significantly alter the order of ventricular recovery.

S-T segment changes were noted infrequently after a double Master exercise test. The significance of these findings should be evaluated in terms of anticipated long term follow-up studies.

In contradistinction to left bundle branch block, right bundle branch block is frequently seen in apparently healthy persons and unless other evidence of heart disease is present or the subject is in the older age group with a previously normal electrocardiogram it should not be accepted as diagnostic evidence of significant underlying heart disease.

References

1. Ferguson, D. O. and O'Connell, J. T. Cardiovascular observations: electrocardiograms of men without heart symptoms. *U. S. Navy M. Bull.*, 24: 860, 1926.
2. Wood, F. C., Wolferth, C. C. and Miller, T. G. Electrocardiography in military medicine. *War Med.*, 1: 696, 1941.
3. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1,000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
4. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew. *Circulation*, 10: 384, 1954.
5. Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
6. Smith, G. B., Jr. and Lamb, L. E. The comparative vectorgram: a simple method for analysis of lead similarity. *Am. J. M. Sc.*, 237: 434, 1959.
7. Lamb, L. E. and Smith, G. B., Jr. A study of the human torso as a volume conductor by comparative vectorgram analysis: the dR factor. *Am. J. M. Sc.*, 237: 612, 1959.
8. Lamb, L. E. and Smith, G. B., Jr. An electrically balanced bipolar vectorcardiographic system: lead analysis and lead synthesis using the dR factor. *Am. J. M. Sc.*, 237: 759, 1959.
9. Lamb, L. E. Fundamentals of Electrocardiography and Vectorcardiography, p. 64. Springfield, Ill., 1957. Charles C Thomas.
10. Rosenman, R. H., Pick, A. and Katz, L. N. Intraventricular block—review of the literature. *Arch. Int. Med.*, 86: 196, 1950.
11. Yater, W. M. Pathogenesis of bundle branch block. *Arch. Int. Med.*, 62: 1, 1938.
12. Graybiel, A. and Sprague, H. B. Bundle branch block; an analysis of 395 cases. *Am. J. M. Sc.*, 185: 395, 1933.
13. Shreenivas, Messer, A. L., Johnson, R. P. and White, P. D. Prognosis in bundle branch block; factors influencing the survival period in right bundle branch block. *Am. Heart J.*, 40: 891, 1950.
14. von Deesten, H. T. and Dolganos, M. Atypical bundle branch block with a favorable prognosis. *Am. J. M. Sc.*, 188: 231, 1934.
15. Willius, F. A., Dry, T. J. and Reeser, R. Life expectancy in conductive disturbances affecting the ventricular complex of the electrocardiogram. *Arch. Int. Med.*, 67: 1034, 1941.
16. Wolfram, J. Bundle branch block without significant heart disease. *Am. Heart J.*, 41: 656, 1951.
17. Wood, F. C., Jeffers, W. A. and Wolferth, C. C. Follow up study of 64 patients with a right bundle branch conduction defect. *Am. Heart J.*, 10: 1056, 1935.
18. Langley, R. W., Reed, J. C. and Utz, D. C. Bundle branch block; a review of 100 cases. *Am. Heart J.*, 33: 730, 1947.
19. Lamb, L. E., Averill, K. H. and Dermksian, G. Intermittent right bundle branch block without apparent heart disease. *Am. J. Cardiol.*, 4: 302, 1959.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

VII. Atrioventricular Block*

MAJ. ROBERT L. JOHNSON, MC, USAF, CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

A SURVEY of the electrocardiograms of 67,375 apparently healthy male fliers revealed 350 cases of first degree A-V block, one case of second degree A-V block with Wenckebach phenomenon and one case of complete A-V block. This large number of subjects with A-V block was identified in a population which was unusual both in its magnitude and its apparent freedom from disease. Previous reports of A-V block in healthy persons[1-3] have usually involved much smaller groups. On the other hand, most large series of patients with A-V block reported on in the literature have come from hospital and clinic populations which include a high proportion with cardiovascular and other organic disease.[4-7] The large number of cases of A-V block identified in the present study provided a unique source of information concerning this conduction abnormality in a healthy population. This report will present certain data and observations concerning A-V block arising from this survey.

MATERIAL AND METHODS

The electrocardiograms of the 67,375 subjects in this study were recorded routinely to fulfill requirements for flying. These records, obtained from asymptomatic, apparently healthy men, were those received by the U. S. Air Force Electrocardiographic Repository during its first eighteen months of existence and represent the first large group of tracings set aside for detailed analysis. A complete description of the survey is reported elsewhere.[8] It should be stressed that the population comprising this survey was a highly select one whose health and physical standards were probably higher than would be found in healthy groups of similar age in the general population.

The routine electrocardiograms were first scanned for significant abnormalities. Those showing P-R intervals of greater than 0.20 second, regardless of heart rate, were arbitrarily classified as examples of first degree A-V block. Although the P-R interval in the precordial leads, usually those over the left precordium, of a few records appeared slightly longer than in the limb leads, only the bipolar or augmented unipolar limb leads were used for this measurement. Occasionally, limb lead I or aVF seemed most suitable, but in most records limb lead II showed most clearly the onset of the P wave and frequently the longest P-R interval. Occasionally, the initial portion of the QRS interval was isoelectric in lead II, producing apparent lengthening of the P-R interval. In such instances the difference between the longest P-S interval and the longest QRS values in the limb leads was used to determine the true P-R interval, as suggested by White and associates.[9]

Clinical Data: Data concerning the subject's age, weight, height, blood pressure and race, which in nearly every case accompanied the electrocardiogram, were tabulated. The records were individually analyzed for duration, amplitude and vector axis of the P wave, and inspected for the occurrence of unusual features and abnormalities other than the A-V conduction defect.

In addition, 139 of the 350 subjects with first degree A-V block were evaluated clinically. Medical personnel at the subject's home base examined 118 subjects. The remaining twenty-one, and two others with higher degrees of A-V block, were seen at the School of Aviation Medicine where the evaluation consisted of a complete history and physical examination, complete hemogram and urinalysis, a twelve-lead electrocardiogram and double Master exercise test taken in the fasting state, x-ray films of the chest in posteroanterior and lateral projections, fasting blood sugar, cholesterol and phospholipid determinations, and special electrocardiographic studies.

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

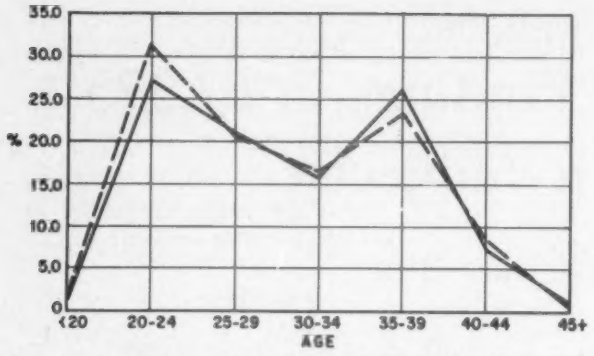


FIG. 1. Incidence of first degree A-V block. The solid line indicates the number of subjects in each five-year age group as percentage of the 67,375 subjects surveyed. The broken line shows the number of subjects with first degree A-V block in each five-year age group as percentage of 350 found in the survey.

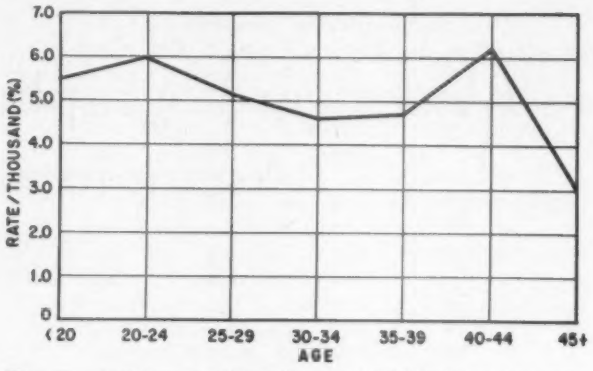


FIG. 2. Incidence of first degree A-V block by five-year age groups expressed as rate per thousand.

Other procedures, such as glucose tolerance test, glucose tolerance electrocardiogram, vectorcardiography, bacteriologic cultures, determination of antistreptolysin titer, transaminase levels, fluoroscopy and additional roentgenologic studies and tests to evaluate physical capacity, were carried out when specifically indicated.

The special electrocardiographic studies were directed to determination of the effect on the cardiac mechanism of orthostatic stresses, various breathing maneuvers, carotid sinus massage, breathing 100 per cent oxygen both at atmospheric and at positive pressure, and of atropine given intravenously. Records were made during periods of maximum breath-holding, and hyperventilation immediately followed by breath-holding, with the subject supine and later while standing. Carotid sinus massage for fifteen seconds while sitting was performed first on the right side and three minutes later on the left side. Positive pressure breathing at 11.2 mm. Hg was accomplished using a pressure-demand mask and regulator at a setting of 43,000 feet. A continuous four-lead electrocardiogram recording leads I, II and III and usually V_2 or V_5 was made prior to each maneuver, throughout its performance, and for an appropriate period after completion of the maneuver. After recording the reactions to these stress procedures, a continuous tracing was made during and for three minutes after 1.2 mg. atropine sulfate was injected intravenously. Thereafter, tracings were taken at one-minute intervals for ten minutes.

Studies similar to these were carried out at the base medical facility of the other 118 subjects with first degree A-V block. Blood phospholipid studies were not performed in most of these subjects and the special electrocardiographic studies were less extensive. The latter included, however, double Master exercise tolerance tests in 112, electrocardiograms while standing in 106, and after administration of atropine (1.2 mg. intravenously) in seventy-three. In a few the effect of respiratory maneuvers and carotid sinus massage was also recorded electrocardiographically.

RESULTS

FIRST DEGREE A-V BLOCK

Age: In the majority of cases, the first knowledge of A-V block was obtained from the record taken for the repository. At this time the ages of the subjects ranged from seventeen to fifty-four years. The incidence of first degree A-V block in the total surveyed population was 5.2 per thousand and it did not appear to change significantly in the different age groups (Figs. 1 and 2). The slight differences in incidence among the various five-year age groups are not statistically significant. The actual number of subjects with first degree A-V block in each five-year age group appears in Table I.

Race: Seven of the 350 subjects were Negroes whose ages ranged from twenty-one to twenty-six years. Calculated on the basis of the total Negro population of 409 in the 67,375 subjects surveyed, this represents an incidence of first degree A-V block in Negroes of 17.1 per thousand.

TABLE I
Age of 350 Subjects with First Degree A-V Block

Age (yr.)	No. of Subjects
Less than 20	7
20–24	109
25–29	72
30–34	48
35–39	82
40–44	30
Over 44	2

TABLE II
Weight of 345 Subjects with First Degree A-V Block

Weight (lb.)	No. of Subjects
110–119	1
120–129	2
130–139	12
140–149	37
150–159	53
160–169	67
170–179	60
180–189	59
190–199	21
200–209	20
210–219	9
220–229	2
230–239	1
240–249	1

Height and Weight: The weight of 345 and height of 344 subjects with first degree A-V block were known. The weight range is expressed in Table II which indicates the actual number of subjects in each ten-pound weight group. The median weight was 170 pounds with half of the subjects weighing between 156 and 184 pounds.

Height ranged from $64^1/_2$ to 77 inches with the median falling at 71 inches. Half the group was between $69^1/_4$ and $72^1/_2$ inches tall. The height and weight of these subjects did not differ from the total population surveyed.

Heart Rate: Heart rate, determined from the standard twelve-lead electrocardiograms of 350 subjects with first degree A-V block, ranged from 36 to 118 per minute. The median rate was 66; half the group had heart rates between 58 and 75 per minute. In only one subject was the heart rate above 110 per minute and in only one was it below 40 per minute (Table III). The distribution of the various heart rates was quite similar to that found in a random sampling of normal subjects from the entire population surveyed.

Sinus arrhythmia, often of pronounced degree, was prominent in a large number of the records showing A-V block. The heart rate in individual records varied more than 10 per cent in 255 of the 350 records, but the relatively short tracing mounted in each of the twelve leads frequently made it impossible to ascertain that these variations were always due to sinus arrhythmia.

Blood Pressure: Blood pressure determinations accompanied the electrocardiographic records of 341 subjects. Mean blood pressure in these subjects was 120/74 mm. Hg. One subject, known to have vascular hypertension, had a blood pressure of 180/100 mm. Hg. There were four whose systolic pressure was between 135 and 150 mm. Hg while all others had systolic pressures below 135 mm. Hg. The diastolic pressure of one other subject was recorded as 110 mm. Hg. Five others had diastolic values ranging from 90 to 100 mm. Hg. Except for these, systolic and diastolic pressure was below 135 and 90 mm. Hg, respectively, in all instances.

TABLE III
Heart Rate in 350 Subjects with First Degree A-V Block

Heart Rate (per min.)	No. of Subjects
30–39	1
40–49	14
50–59	84
60–69	120
70–79	85
80–89	30
90–99	11
100–109	4
110–119	1

P-R Interval: The P-R interval in the 350 subjects with first degree A-V block ranged from 0.21 to 0.39 second. Table IV shows durations of the P-R intervals observed and the number of subjects showing each of these values.

TABLE IV
Duration of P-R Interval in 350 Subjects with First Degree A-V Block

P-R Interval (sec.)	No. of Subjects
0.21	35
0.22	85
0.23	70
0.24	90
0.25	14
0.26	18
0.27	4
0.28	19
0.29	2
0.30	3
0.32	4
0.36	4
0.39	2

TABLE V
P-R Interval for Each Five-Year Age Group in 350 Subjects with First Degree A-V Block

P-R Interval (sec.)	No. of Subjects in Each Five-Year Age Group (yr.)							Total
	Less than 20	20–24	25–29	30–34	35–39	40–44	Over 45	
0.21	0	8	9	8	7	2	1	35
0.22	2	23	19	10	21	10	0	85
0.23	0	21	12	7	21	9	0	70
0.24	4	29	16	15	21	4	1	90
0.25	0	3	5	0	2	4	0	14
0.26	1	7	4	3	3	0	0	18
0.27	0	3	0	1	0	0	0	4
0.28	0	8	3	2	6	0	0	19
0.29	0	1	0	0	1	0	0	2
0.30	0	3	0	0	0	0	0	3
0.32	0	1	3	0	0	0	0	4
0.36	0	1	1	1	0	1	0	4
0.39	0	1	0	1	0	0	0	2

Table v depicts the same information tabulated according to five-year age groups. Except for a possible tendency for P-R values of 0.20 second or greater to occur more often in the younger age groups, no relation between age and the duration of P-R interval was evident. Similarly, the duration of the P-R interval seemed to be unrelated to the heart rate (Table VI). There was no apparent tendency for the longest P-R intervals to occur in association with the slowest heart rates.

In records with marked sinus arrhythmia there was no consistent relation between the length of the P-R and R-R intervals. In most subjects with first degree A-V block and sinus arrhythmia, the P-R interval showed no appreciable change with fluctuations in heart rate. In others the P-R interval increased slightly as heart rate slowed. Approximately the same number of subjects showed slight decrease in the duration of the P-R interval during the slow phase of sinus arrhythmia.

P Wave: Duration of the P wave was determined in the lead used for measurement of the P-R interval, usually limb lead II. As shown in Table VII, duration of the P wave ranged from 0.07 to 0.16 second, with most records having values of from 0.10 to 0.12 second;

TABLE VI
Heart Rate and P-R Interval in 350 Subjects with First Degree A-V Block

P-R Interval (sec.)	No. of Subjects and Heart Rates								
	30–39	40–49	50–59	60–69	70–79	80–89	90–99	100–109	110–119
0.21	...	...	8	10	9	2	2	3	1
0.22	...	2	19	32	21	8	2	1	...
0.23	...	4	17	23	19	5	2	...	...
0.24	1	6	21	26	24	11	1	...	...
0.25	...	1	4	5	2	1	1	...	...
0.26	...	...	6	8	3	1	...	...	...
0.27	...	...	1	3	...	...	...	...	...
0.28	...	1	4	7	3	1	3	...	...
0.29	...	...	1	...	1	...	...	...	...
0.30	...	...	...	2	1	...	...	...	...
0.32	...	...	1	2	...	1	...	...	...
0.36	...	...	2	...	2	...	...	...	...
0.39	...	...	...	2	...	...	...	...	...

TABLE VII
Duration of P Wave in 350 Subjects with First Degree A-V Block

P Wave Duration (sec.)	No. of Subjects
0.07	1
0.08	7
0.09	18
0.10	101
0.11	107
0.12	95
0.13	16
0.14	3
0.15	1
0.16	1

the mode was 0.11 second. Although slightly higher than the average value usually given for P wave duration, the subjects with first degree A-V block did not differ appreciably with respect to P wave duration from others in the surveyed population of 67,375 subjects. The P wave exceeded 0.12 second in duration in twenty-one records. The subject whose P wave measured 0.16 second had a P-R interval measuring 0.22 second and therefore did not demonstrate true A-V block despite prolongation of the P-R interval. The same question might arise in one subject whose P wave measured 0.14 second and who had a P-R interval of 0.23 second, and in perhaps some of those whose P wave duration was 0.13 second. Of the sixteen subjects having the latter value for P wave duration, there were two with P-R intervals of 0.21 second, three with 0.22 second, three with 0.24 second and one with 0.25 second. Others whose P wave duration exceeded 0.12 second showed P-R intervals of 0.26 second or greater. In the ninety-five records with P wave duration of 0.12 second, the P-R interval was 0.21 in nine, 0.22 in twenty, 0.23 in eighteen and 0.24 second or more in the remaining records.

The amplitude of the P wave was within normal limits in all instances. In two records the amplitude was 0.25 mv. but in all others the amplitude was less, as shown in Table VIII. In a few records slight irregularity or notching of the P wave was apparent. In no instance was this characteristic sufficiently pronounced to arouse suspicion of abnormality.

The mean P vector axis in the frontal plane was found to lie between +15 and +75 degrees in

TABLE VIII
Amplitude of P Wave in 350 Subjects with First Degree A-V Block

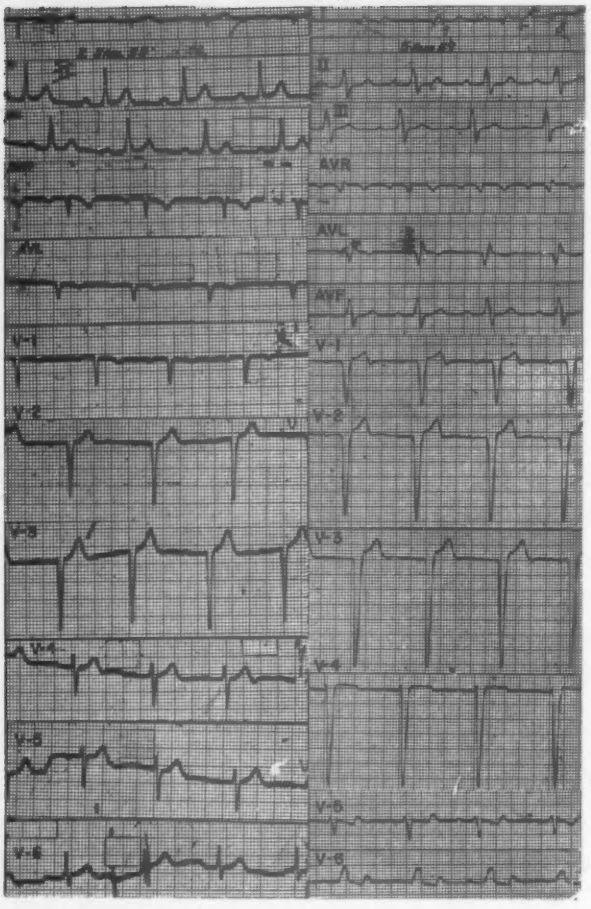
Amplitude (mv.)	No. of Subjects
0.05	116
0.10	172
0.15	50
0.20	10
0.25	2

343 subjects, at zero degrees in three, and at −30 degrees in one (Table IX). Four subjects with atrial rhythm had P waves whose vector axes were at −45 and −75 degrees, with negative deflections therefore appearing in all limb leads except I and aVL. P-R intervals in these four records were 0.23 second or longer in duration. In one of these four, this lower pacemaker alternated rhythmically with a normal sinus pacemaker, the latter appearing only during the slightly faster heart rate associated with inspiration. Here the P-R interval following the sinus P wave was of normal duration while that following the lower pacemaker was prolonged to 0.23 second.

Other Electrocardiographic Findings: One subject, aged forty-four, had complete right bundle branch block with prolongation of the QRS complex to 0.12 second and of the P-R interval to 0.24 second. These intervals had remained unchanged since discovery when the subject was forty years old. Delay in intraventricular conduction with QRS duration not exceeding 0.12 second was present in six records. Two of the latter contained R′ waves in precordial lead V_1 and were categorized as delay in conduction

TABLE IX
P Vector Axis in Frontal Plane in 350 Subjects with First Degree A-V Block

Axis (degrees)	No. of Subjects
−75	1
−45	3
−30	1
0	3
+15	14
+30	36
+45	113
+60	84
+75	95



A B

FIG. 3. Routine electrocardiograms. A, initial tracing (lead aVF missing). B, tracing taken nineteen months later at time of clinical evaluation. Both show inverted P waves in lead V_1, failure of progression of R in leads V_1 through V_3, and prolonged A-V conduction (P-R interval = 0.24 to 0.26 second). The later tracing also shows complete left bundle branch block.

over the right ventricle. Eleven records showed an $S_1S_2S_3$ pattern with R′ waves in precordial lead V_1. The mean QRS vector axis was +135 degrees in one of these. In all other records the QRS and T vectors were directed normally. Two records showed flattening of T waves, non-specific in type, which were not considered definitely indicative of disease.

Presence of Disease: At the time of clinical evaluation of the 139 subjects examined, usually from four to sixteen months after the initial repository records had been taken, only five of the 139 subjects, all thirty-six years of age or older, showed symptoms or signs indicating organic disease.

1. One was a fifty-two year old officer who for several years had been known to have mild hypertension and first degree A-V block. The A-V block was persistent with the P-R interval measuring 0.24 second. Although diastolic blood pressure was always approximately 100 mm. Hg, he had remained asymptomatic and was otherwise free of demonstrable hypertensive complications.

2. A thirty-eight year old pilot related recurring discomfort in the chest of several weeks' duration. This discomfort was not typical of angina nor were there changes in his electrocardiogram suggesting coronary artery disease. The occurrence of a myocardial infarction could not be substantiated, but it was believed that coronary artery disease was responsible for the pain in the chest. The first degree A-V block in the repository tracing taken eighteen months earlier was still present.

3. A third pilot, aged thirty-six, exhibited complete left bundle branch block in the electrocardiogram taken during his evaluation. His repository record, taken eighteen months earlier, had shown first degree A-V block with a P-R interval of 0.25 second and a normal QRS duration. In both tracings (Figs. 3A and B) there was failure of progression of R waves in precordial leads V_1 through V_3. The P waves were inverted in leads V_1 and V_2, indicating that the electrodes were high in relation to the usual position of the heart. He was asthenic in stature; 6 feet tall and weighed 143 pounds. The question may be raised as to whether or not asymptomatic anterior infarction prior to the first tracing might be responsible for the abnormal appearance of the QRS complexes in the right chest leads. The inverted P waves and possible misplacement of electrodes complicate the interpretation. He was asymptomatic in the interval between the two records. His past history was one of excellent health. Neither the physical examination, laboratory determinations nor special electrocardiographic studies revealed other evidence of disease, the electrocardiographic findings of A-V block, left bundle branch block and the failure of R wave progression in the right chest lead constituting the sole abnormalities. Despite lack of other evidence, the most likely explanation for the appearance of left bundle branch block during the eighteen-month interval was the presence of significant and progressive coronary artery disease with the added possibility of a remote asymptomatic anterolateral septal infarction.

4. Definite organic disease not primarily of a cardiovascular nature developed in two other subjects. One of these, a thirty-nine year old man with a history of acute hepatitis fifteen years earlier, began to experience symptoms typical of diabetes mellitus about one year after his baseline repository electrocardiogram had been taken. Diagnosis of the diabetic state was confirmed and insulin therapy was instituted. After the first month, dietary measures alone were sufficient for control. At the time of evaluation for first degree A-V block his electrocardiogram was unchanged, showing no abnormality other than the

prolongation of the P-R interval to 0.24 second. The only objective evidence of diabetes mellitus at this time, one year after the onset of symptoms, was a diabetic curve in the glucose tolerance test. In this case, the age of the subject and presence of diabetes favored the view that arteriosclerotic heart disease was responsible for the prolonged A-V conduction time.

5. The fifth person found to have organic disease at the time of evaluation for first degree A-V block was a forty-one year old pilot who experienced hematemesis from an unsuspected and relatively asymptomatic duodenal ulcer. This episode occurred about one year after the recording of the electrocardiogram which showed prolongation of the P-R interval to 0.23 second. His resting electrocardiogram, taken two months after hospitalization for hematemesis, was unchanged. At this time, tracings taken immediately after standing and after a double Master exercise test showed A-V dissociation.

Historical Data: Beside the symptomatology already noted in those with definite disease, the remaining subjects with first degree A-V block were free of symptoms. When present, symptoms were vague and non-specific and did not interfere with flying duties or strenuous physical activity. The subject with right bundle branch block and prolonged A-V conduction was asymptomatic and without evidence of disease except for the abnormal electrocardiogram.

The past histories were not unusual or particularly different from those which might be seen in any similar group. Two subjects gave a history of acute rheumatic fever with joint manifestations during early childhood. Another was told that he had chorea in childhood. One had a history at age twenty-seven of a rheumatic type of illness, thought to be rheumatoid arthritis, which lasted several weeks and occurred about one year before recording of his repository electrocardiogram. However, an electrocardiogram taken several years earlier had also shown first degree A-V block.

There was a past history of diphtheria in three, scarlet fever in fourteen, pneumonia in seven and pleurisy in three others. Mumps had occurred in sixty-seven and in two had been complicated by orchitis and pancreatitis, although apparently not by myocarditis or pericarditis. Two had illnesses in early adulthood suggestive of pericarditis. There was a history of acute hepatitis and/or jaundice in three, illnesses within the past two years diagnosed as infectious mononucleosis in two and malaria in three. Thoracic surgery had been performed in one subject for pulmonary tuberculosis with subsequent arrest, and in another for recurrent pneumothorax. Two had recent histories of vascular "cluster" headaches.

Family histories were also of interest but noncontributory in relation to the A-V block. In ten subjects there were histories of death in the immediate family due to acute coronary disease. Fatal coronary occlusion had occurred at age thirty-six in the father and at about forty in an uncle of one, and the brother of another subject had died at age thirty-four after a second myocardial infarction. Rheumatic heart disease had been recognized in the parents of three of these subjects. In eight others there were non-specific histories of heart disease in parents or siblings. In six there was known diabetes mellitus in parents or grandparents.

Physical Findings: Physical examinations were no more revealing than the histories in producing information that might relate to the A-V conduction disturbance. Only two subjects had systolic murmurs sufficiently loud to be classed as grade 2 in intensity. These were located at the apex in one and along the left sternal border in the other. Neither was associated with demonstrable cardiac enlargement by roentgenography and fluoroscopy, or by other clinical evidence of cardiac disease. Two subjects had transistory elevation of blood pressure which was attributed, after investigation, to vascular hyperreactivity. Three had moderate degrees of pectus excavatum. With these exceptions, all 139 subjects had normal findings on complete physical examination.

Laboratory Data: Routine hemograms and urinalyses were within normal limits, as were fasting blood sugar levels. Cultures from throat smears, antistreptolysin titers, and transaminase level determinations were carried out only when there seemed to be a clinical indication for obtaining them; none was positive. Serologic tests for syphilis were negative in all instances. Posteroanterior and lateral x-ray films of the chest showed no cardiac abnormality or evidence of pulmonary disease which could not be explained as residual of disease recognized and treated in the past.

Blood cholesterol determinations were made in 131 of the 139 subjects at the time of their clinical evaluation. These values ranged from 130 to 348 mg. per cent with the median between 200 and 225. Table x shows the distribution of the various cholesterol values. Elevations of

TABLE X

Serum Cholesterol Levels in 131 Subjects with First Degree A-V Block

Cholesterol (mg. %)	No. of Subjects
126–150	5
151–175	16
176–200	27
201–225	29
226–250	20
251–275	13
276–300	12
301–325	6
326–350	3

TABLE XI

Mean Serum Cholesterol Levels for Each Five-Year Age Group in 131 Subjects with First Degree A-V Block

Age (yr.)	No. in Group	Mean Cholesterol (mg. %)
Less than 20	1	212
20–24	27	207
25–29	25	210
30–34	24	252
35–39	37	227
40–44	16	211
Over 44	1	250

blood cholesterol to more than 300 mg. per cent were found in nine subjects. There was no consistent tendency within the group for cholesterol levels to rise with increasing age (Table XI).

Phospholipid levels were determined in twenty-six subjects; the range was from 132 mg. to 327 mg. per cent with a mean of 229.

Exercise Tolerance Test: A double Master exercise test was performed in the standard manner by 136 of the subjects who were examined clinically. Using as the criteria for a positive test a plateau-type S-T segment depression of at least 1 mm. occurring in any lead and persisting at least into the two-minute tracing, it was found that all these subjects responded normally.

Electrocardiographic Changes: Clinical evaluation of the 139 subjects whose repository electrocardiograms showed first degree A-V block revealed that the block had been replaced by normal A-V conduction times in thirteen at the time of the later tracing. An average time of sixteen months had lapsed between the two sets of tracings. In two of these subjects the change was minimal, from 0.21 second originally to 0.20 second in the later records. The tracings of two others showed reductions in the P-R interval from 0.22 to 0.20 second. The greatest change was seen in two subjects whose initial records had shown P-R intervals of 0.28 second, and who later had P-R intervals of 0.20 and 0.18 second. In the other seven the P-R interval had shortened from 0.03 to 0.05 second. Generally the heart rates in the two sets of records were quite similar. In none did the history indicate the presence of infection or point to other factors which might have caused transient prolongation of conduction time when the repository records were made.

When attention was centered on the subjects

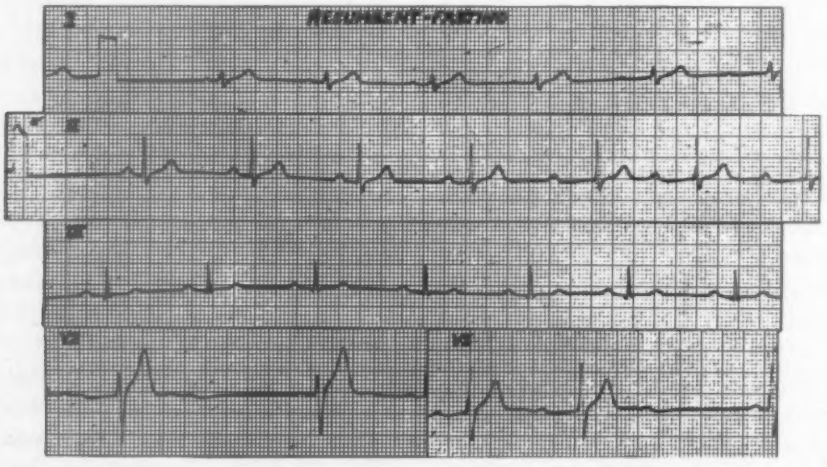


FIG. 4. Baseline tracing prior to exercise tolerance test showing second degree A-V block with Wenckebach periods. Blocked P waves occur at beginning of lead II (superimposed on standardization mark), and in leads V_2 and V_5.

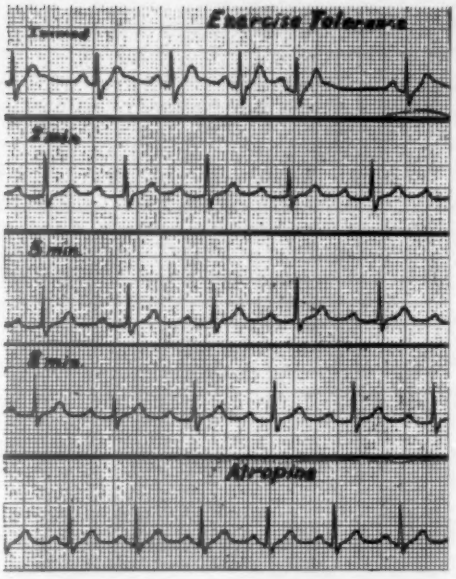


FIG. 5. Exercise tolerance test and tracing after administration of atropine from same subject as in Figure 4. Exercise has abolished second degree A-V block with Wenckebach periods present in baseline tracing. The tracings immediately after exercise and after administration of atropine show normal P-R intervals.

with greater degrees of A-V prolongation it was noted that twenty-five subjects who initially had P-R intervals of 0.25 second or more had been evaluated clinically. Of these twenty-five, there were eleven in whom the P-R interval at time of evaluation was found reduced to 0.24 second or below with three showing decreases to normal values. Three of the original twenty-five, on the other hand, showed increases of P-R interval amounting to from 0.06 to 0.12 second. In addition, there were fourteen other subjects whose initial P-R intervals of from 0.22

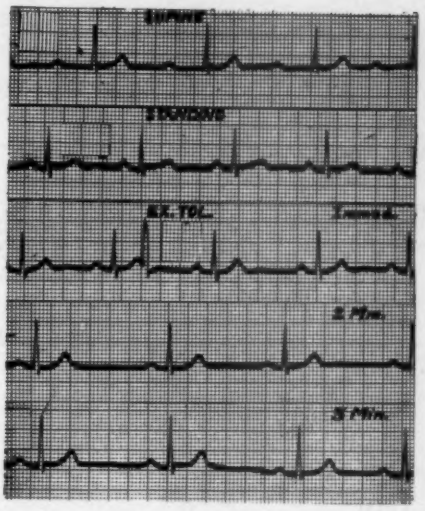


FIG. 6. Electrocardiogram, lead II, showing reduction of P-R interval from 0.39 to 0.41 second to normal after standing and after exercise. The third large deflection in the record immediately after exercise is a standardization mark.

to 0.24 second had increased an average of slightly over 0.03 second. Among the twenty-five with P-R intervals initially measuring 0.25 second or more who were subsequently evaluated, two were found to have evidence of organic cardiac disease: the subject in whom complete left bundle branch block developed and the one believed to have anginal symptoms. Both had P-R intervals of 0.25 second in their repository tracing. Most of the subjects had P-R intervals identical to or approximately the same as in their original repository tracings.

One subject, twenty-six years old, who had a P-R interval of 0.22 second in his initial repository record, demonstrated intermittent second degree

TABLE XII
Effect of Standing on P-R Interval

P-R Interval Recumbent Baseline (sec.)	No. of Subjects	Per Cent of Subjects with P-R Interval			
		Unchanged	Decreased		
			0.02–0.05 sec.	0.06–0.10 sec.	>0.10 sec.
<0.21	10	50	50	0	0
0.21–0.23	65	24.5	72.4	3.1	0
0.24–0.26	31	6.5	71	23.5	0
0.27–0.29	10	0	60	40	0
>0.29	11	0	0	36.4	63.6
Total	127	18.1	63	13.4	5.5

TABLE XIII
Effect of Exercise on P-R Interval

P-R Interval Recumbent Baseline (sec.)	No. of Subjects	Per Cent of Subjects with P-R Interval				
		Unchanged	Increased >0.02 sec.	Decreased		
				0.02–0.05 sec.	0.06–0.10 sec.	>0.10 sec.
<0.21	11	9.1	9.1	81.8	0	0
0.21–0.23	69	13.1	4.3	69.5	13.1	0
0.24–0.26	32	3.1	0	68.8	28.1	0
0.27–0.29	10	0	0	50	40	10
>0.29	11	0	0	18.2	36.4	45.4
Total	133	8.3	3.1	64.6	19.5	4.5

A-V block during clinical evaluation. His routine twelve-lead electrocardiogram showed only first degree A-V block, but his resting record prior to the exercise tolerance test (Fig. 4) showed second degree A-V block with Wenckebach phenomenon, the P-R interval increasing from 0.15 second to 0.42 second. In the postexercise record (Fig. 5) and other tracings only first degree A-V block was present. His past history was non-contributory except that he was one of the two subjects who gave a history of mumps complicated by orchitis. There was no history of illness in recent years and he was asymptomatic. Complete clinical studies failed to reveal other evidence of significant disease.

Response of P-R Interval to Stress. Body Position: During their clinical evaluations, twelve-lead electrocardiograms were obtained both *while recumbent and while standing* in 127 of the 139 subjects. In twenty-three of these the P-R interval was unchanged or changed no more than 0.01 second after standing. In the other 104 subjects standing resulted in an appreciable shortening of the A-V conduction time. An example of marked shortening of the P-R interval after standing and after an exercise tolerance test is shown in Figure 6. Reduction of more than 0.06 second was observed in twenty-four. The changes in duration of the P-R interval in response to orthostatic influences are shown in Table XII. The greatest change was usually seen in the tracing taken within the first minute of standing. Measurements were made in the same lead, usually lead II, while standing as had been used for measurement in the recumbent tracing.

Exercise: The P-R intervals were measured in the same leads of the baseline resting and the postexercise tracings of the 133 subjects

TABLE XIV
Effect of Atropine on P-R Interval

P-R Interval Recumbent Baseline (sec.)	No. of Subjects	Per Cent of Subjects with P-R Interval			
		Unchanged	Decreased		
			0.02–0.05 sec.	0.06–0.10 sec.	>0.10 sec.
<0.21	1	0	100	0	0
0.21–0.23	49	12.2	61.3	26.5	0
0.24–0.26	24	0	45.8	50	4.2
0.27–0.29	10	0	20	30	50
>0.29	10	0	10	10	80
Total	94	6.4	47.8	30.9	14.9

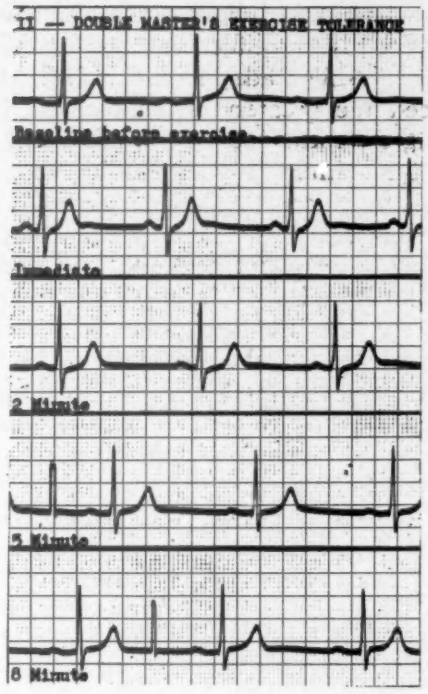


FIG. 7. First degree A-V block with P-R interval 0.26 to 0.28 second (lead II). Marked shortening of P-R interval after exercise.

who performed double Master exercise tests. Usually the record taken immediately after exercise showed the greatest change in the P-R interval, but occasionally this occurred in the two-minute record. By five or eight minutes the typical finding was a return of the P-R interval to nearly baseline values and occasionally to longer than this. In eleven subjects either no change in the P-R interval or a change not exceeding 0.01 second was observed. A shortening of the P-R interval of from 0.02 to 0.05 second occurred in eighty-six subjects while a reduction of 0.06 second or more was seen in twenty-six subjects. A pronounced reduction in P-R interval after exercise is illustrated in Figure 7. In four subjects an increase in the duration of the P-R interval of 0.02 second in two, 0.05 in one, and 0.07 second in the fourth was observed. While it is possible that a shortening of the P-R interval occurred between the time of the immediate and the two-minute tracing in these subjects, such lengthening of the P-R interval after exercise was not seen in the other subjects. The effect of exercise on the P-R interval of 133 subjects is shown in Table XIII.

Atropine: The effect of atropine sulfate, 1.2 mg. given intravenously, was recorded in ninety-four of the 139 subjects. Atropine was not given to several whose P-R interval was normal or only slightly prolonged, and to several others whose P-R interval had become normal after standing or exercise. In six of ninety-four subjects, no change in the P-R interval occurred after administration of atropine. Of the other eighty-eight, forty-four showed reduction of the P-R interval by 0.06 second or more. The effect of atropine on the P-R interval is shown in Table XIV. Table XV compares the effect of administration of atropine, exercise and standing on the P-R interval, eliminating subjects who no longer showed prolongation of A-V conduction time when clinical evaluation was carried out. Figure 8 illustrates marked shortening of A-V conduction time after administration of atropine, considerable shortening after standing and only slight to moderate after the exercise tolerance test in the same subject.

The mean reduction in P-R interval was greater after administration of atropine than that seen either after standing or exercise. The mean reduction in P-R interval after standing, exercise and administration of atropine was 0.04 second, 0.043 and 0.06 second, respectively. Individual variations in response

TABLE XV
Effect of Standing, Exercise and Atropine on P-R Interval of Subjects with First Degree A-V Block

Maneuver or Agent	No. of Subjects	Per Cent of Subjects with P-R Interval				
		Unchanged	Increased	Decreased		
				0.02–0.05 sec.	0.06–0.10 sec.	>0.10 sec.
Standing	117	15.4	0	64.1	14.5	6
Exercise	122	8.2	2.5	63.1	21.3	4.9
Atropine	93	6.5	0	47.4	31.2	14.9

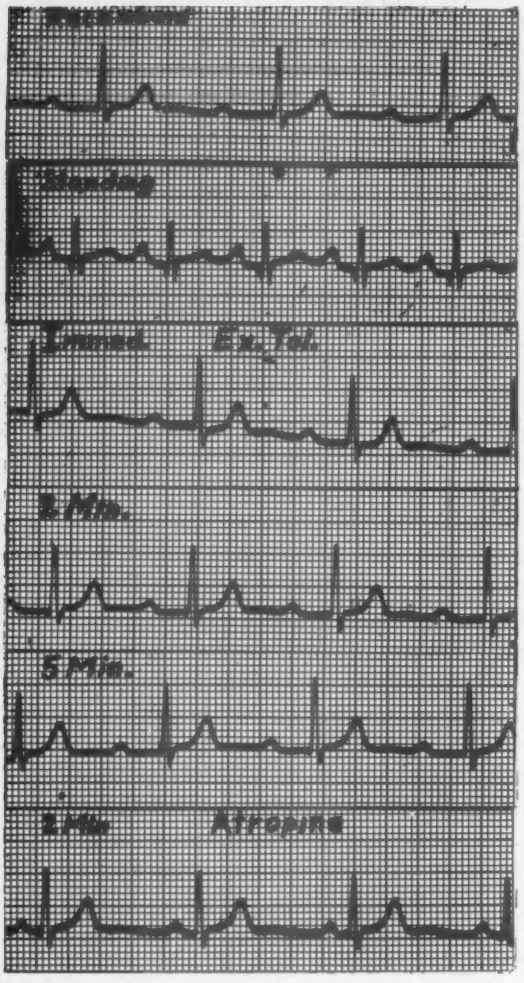


FIG. 8. First degree A-V block with P-R interval 0.33 second (lead II). A-V conduction time reduced to normal after administration of atropine, nearly to normal after standing and only moderately after exercise.

of P-R were marked, however, with a few showing the greatest reduction after standing or exercise. While administration of atropine produced the greatest mean decrease in P-R interval, the mean increase in heart rate at the time of maximum P-R reduction was not as great as that occurring after exercise. This is partly explained by the observation that, following injection of atropine, the maximum reduction in the P-R interval sometimes preceded the maximum increase in heart rate. In a few subjects the P-R interval shortened rapidly, reaching its lowest values during the transient slowing of heart rate that frequently occurs within several seconds after intravenous injection of atropine.

A-V conduction time was reduced to 0.20 second or less in eighty-two of ninety-three (88 per cent) subjects given atropine, in ninety of 122 (74 per cent) after exercise, and in eighty of 117 (68 per cent) after standing. Ninety-one subjects were tested by all three of these procedures. In four of these none of the procedures produced a decrease of the P-R interval to 0.20 second or less. These four showed resting heart rates of 75, 69, 65 and 72 per minute with P-R intervals of 0.32, 0.27, 0.28 and 0.23 second, respectively. The only clinical feature apparently shared by all four was that they were from thirty-six to forty years of age. All others showed a significant reduction of P-R interval after at least one or two procedures and frequently with all three.

Respiratory Maneuvers: The P-R interval often changed in response to breathing maneuvers. These results were not tabulated since records showing these maneuvers were complete

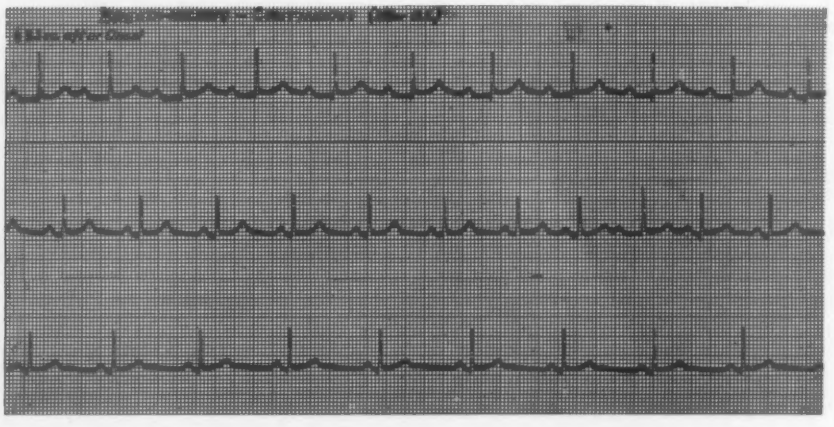


FIG. 9. Continuous record of lead II after breath-holding has been initiated following a period of hyperventilation. The P-R interval shortens progressively, reaching normal in the second strip. Prolongation then occurs transiently and is again followed by normal P-R intervals.

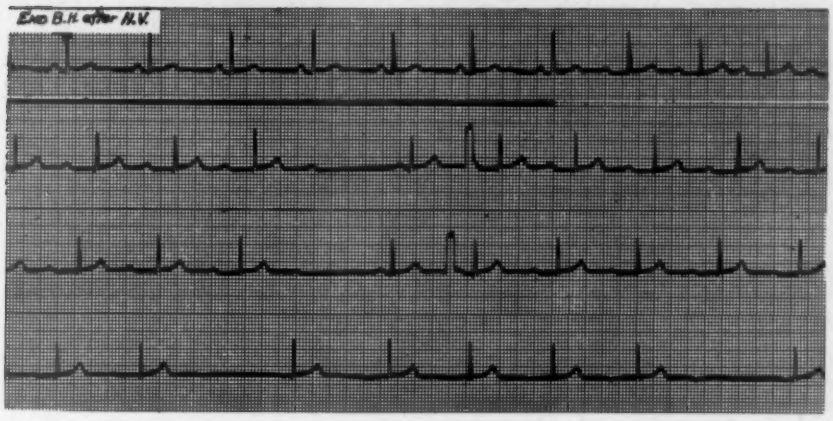


FIG. 10. Continuous record of lead II in same subject as in Figure 9. End of breath-holding (at seventh QRS complex) in first strip is associated with immediate lengthening of P-R interval and second degree block with Wenckebach periods. In the last strip the P waves become inverted, indicating an atrial focus, with second degree block and Wenckebach periods continuing as before.

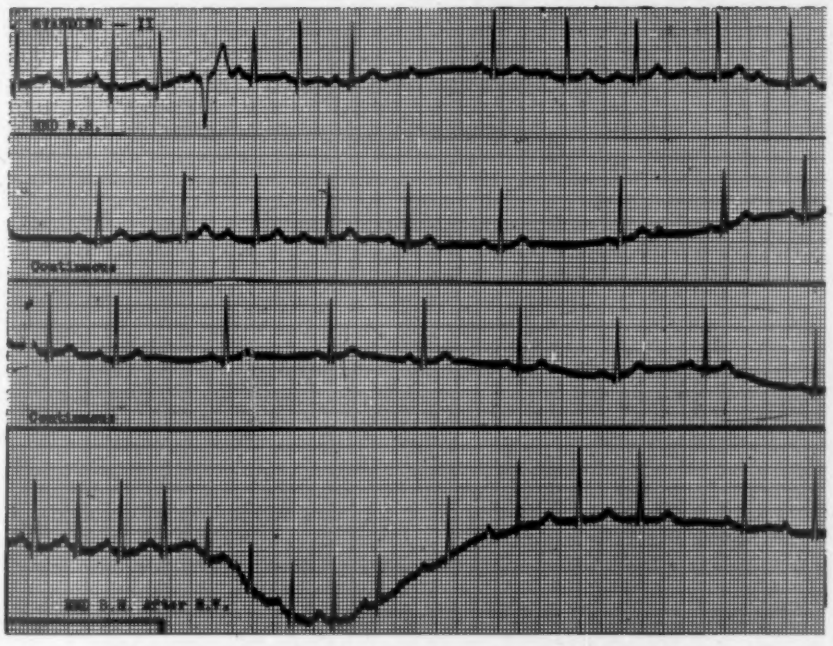


FIG. 11. Continuous record of lead II after release of breath-holding in upper three strips. Fourth strip taken at end of breath-holding after a period of hyperventilation. A fusion beat, marked variation in P-R interval and two blocked atrial impulses appear after the first maneuver. After the second maneuver vagal effects are less pronounced.

only in the twenty-one subjects evaluated at the School of Aviation Medicine. It was noted, however, that A-V conduction time frequently lengthened appreciably at the height of the deep inspiration just prior to breath-holding. At this time blocking of sinus impulses was sometimes observed. During the ensuing period of breath-holding, it was usual for the P-R interval to decrease and remain shortened and after termination of breath-holding, to lengthen transiently to values greater than those in the baseline record (Fig. 9).

This effect as well as the appearance of second degree A-V block with Wenckebach phenomenon after release of prolonged breath-holding following a period of hyperventilation is shown in Figure 10. Also, the pacemaker later shifts to a focus lower in the atrium but continues to show Wenckebach phenomenon and blocked impulses. Figure 11 illustrates a similar increase in the degree of A-V block after breath-

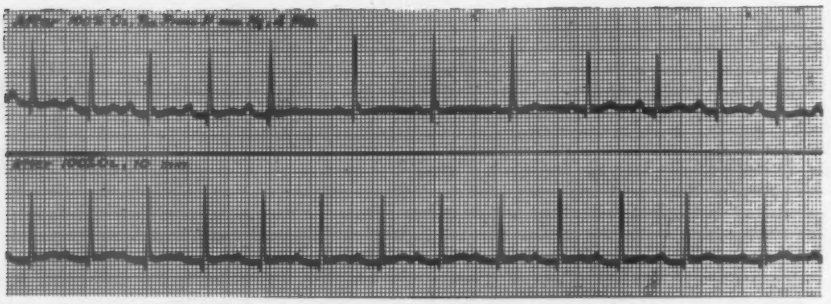


FIG. 12. Electrocardiogram, lead II, from the same subject while breathing 100 per cent oxygen at positive pressure (*upper strip*) and at atmospheric pressure (*lower strip*). Intermittent reduction of A-V conduction time occurs during positive pressure breathing.

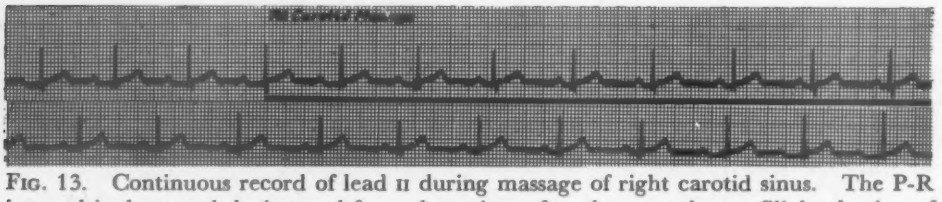


FIG. 13. Continuous record of lead II during massage of right carotid sinus. The P-R interval is shortened during and for a short time after the procedure. Slight slowing of heart rate occurs as expected, although the effect on the P-R interval is opposite to that usually seen.

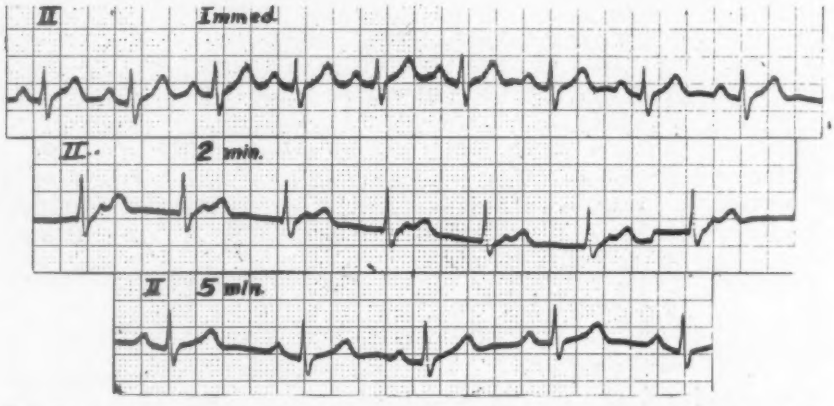


FIG. 14. Electrocardiogram, lead II, after a double Master exercise test. A-V dissociation is seen two minutes after exercise. The P-R interval before exercise was 0.25 second.

holding in another subject. Pressure breathing with 100 per cent oxygen generally produced more marked changes in P-R interval and heart rate than breathing 100 per cent oxygen at atmospheric pressure, suggesting that pulmonary stretch reflexes or mechanical alterations of pulmonary and cardiac hemodynamics were responsible for these changes (Fig. 12). Shortening of the P-R interval sometimes occurred during carotid sinus massage whether or not significant slowing of heart rate was produced (Fig. 13), although it was more usual to see the expected increase in the P-R interval during this procedure.

Arrhythmias in Response to Stress Maneuvers: As a group, an increased tendency for cardiac arrhythmias and shifts in the pacemaker to develop was seen in the subjects with A-V block as compared with other subjects observed who underwent the same type of tests.

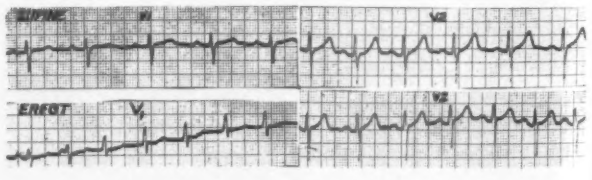


FIG. 15. Precordial leads V_1 and V_2 in one subject while supine (*upper two strips*) and while erect (*lower two strips*). Lead V_1, taken while standing, shows the onset of A-V dissociation which was of brief duration. The P-R interval became normal in the erect position.

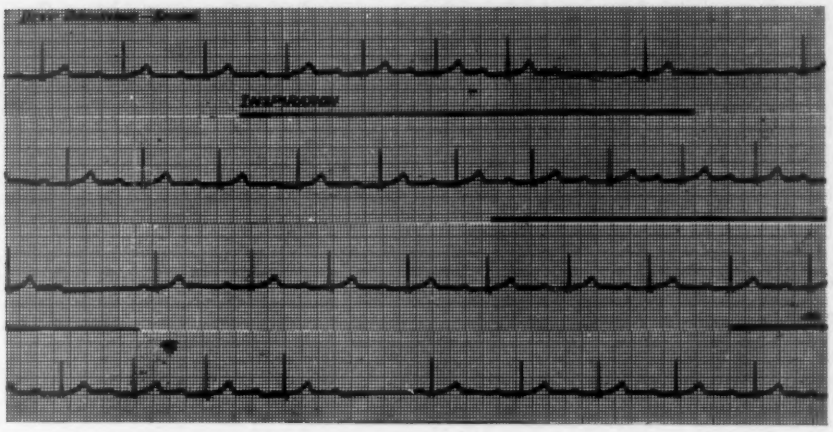


FIG. 16. Continuous record of lead II during deep, slow breathing with the subject supine. Atrial impulses are blocked at the height of inspiration during each respiratory cycle. The P-R interval following each blocked atrial impulse is of normal duration. The other P-R intervals during each respiratory cycle vary only slightly.

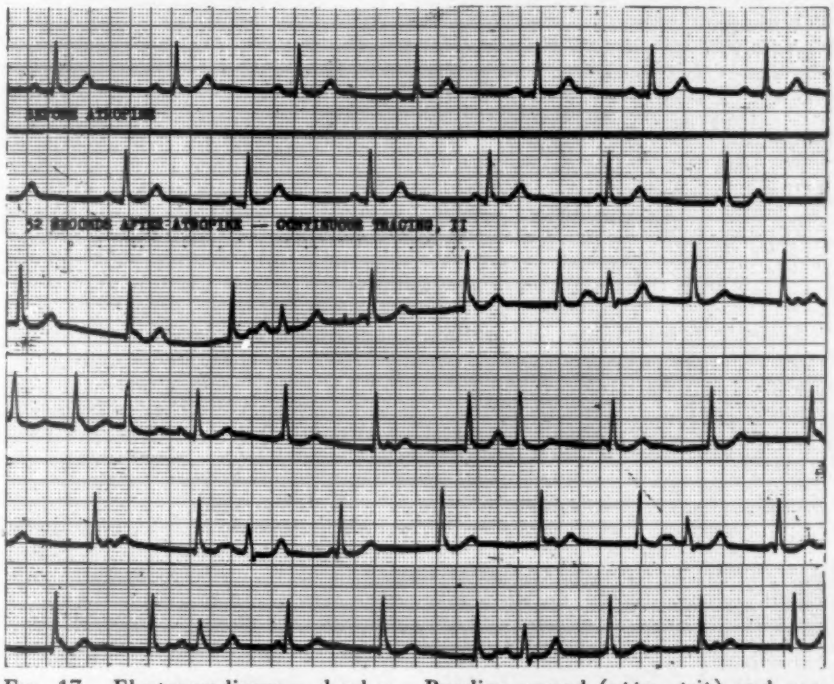


FIG. 17. Electrocardiogram, lead II. Baseline record (*upper strip*) and continuous tracing beginning thirty-two seconds after intravenous injection of 1.2 mg. atropine sulfate (*lower five strips*). A-V dissociation with ventricular capture occurring frequently. The P wave appears to "march" rapidly through the QRS complex to the T wave where it appears sufficiently late to permit conduction to the ventricles.

Two of the subjects showed A-V dissociation after the exercise tolerance test and one of these also showed this phenomenon after standing (Figs. 14 and 15). Figure 16 shows changes in P-R interval and blocking of sinus impulses during deep, slow and regular breathing. The greatest degree of vagal inhibition is apparent at the height of inspiration. Blocking of sinus impulses with failure of a ventricular response was observed in two subjects during the period immediately following the release of prolonged breath-holding; both had P-R intervals of about 0.30 second in their resting electrocardiograms. Two others showed intermittent atrial rhythm developing at the height of inspiration prior to breath-holding, during breath-holding and after exercise when the heart rate had again begun to decline. Two of the twenty-one showed intermittent second degree A-V block with Wenckebach phenomenon after exercise, at the height of inspiration prior to breath-holding and after the release of breath-holding. Nodal

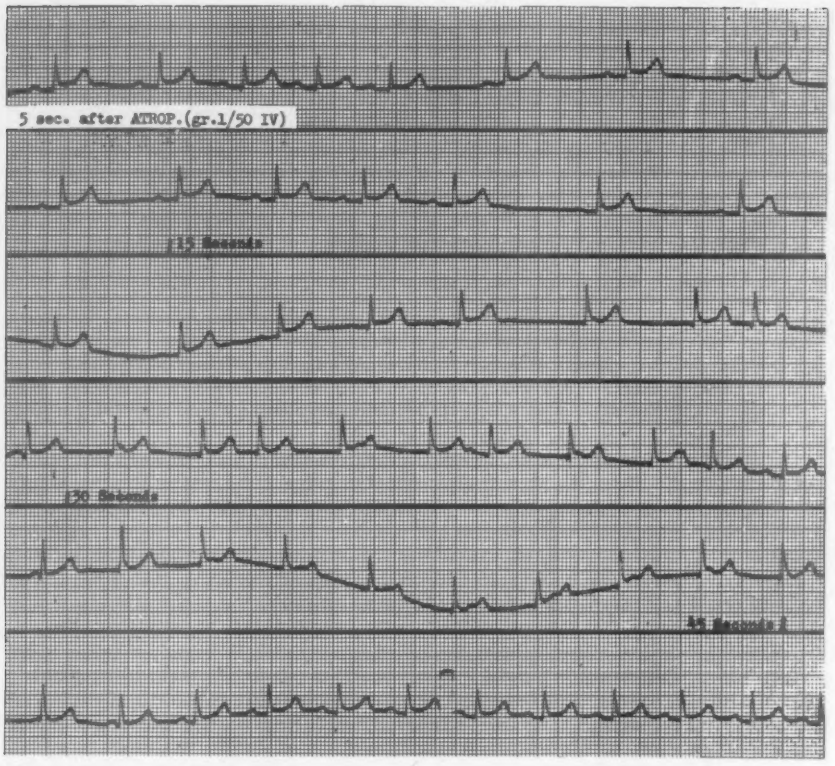


FIG. 18. Continuous record of lead II after intravenous administration of atropine in another subject. A-V dissociation appears about twenty-five seconds after the injection of atropine and lasts for about twenty-five seconds. Ventricular capture occurs frequently.

escape beats were observed during these periods in one of these.

In the twenty-one subjects examined at the School of Aviation Medicine, A-V dissociation of the interference type occurred with about the same frequency as was observed in other subjects without conduction disturbances. In several instances, when A-V dissociation followed the injection of atropine in the subjects with A-V block, P waves occurred unusually late with respect to the QRS complex (Figs. 17 and 18). The P wave in these subjects frequently appeared on the descending portion of the T wave and was sufficiently late to result in ventricular capture. This particular characteristic of A-V dissociation has not been frequently seen after administration of atropine in this laboratory in subjects without A-V conduction defects.

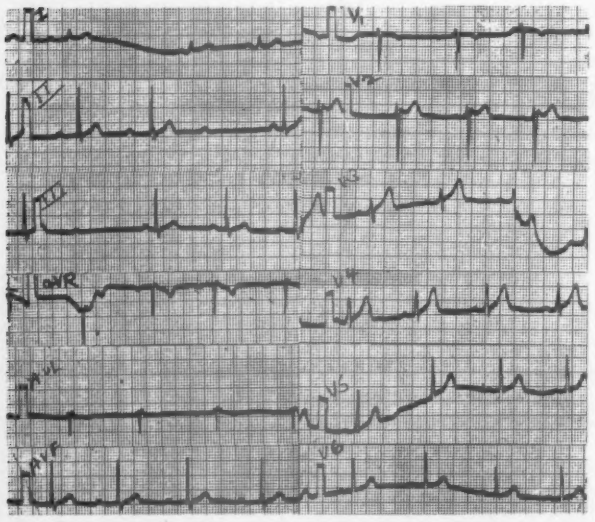


FIG. 19. Routine repository electrocardiogram showing second degree A-V block with Wenckebach periods.

SECOND DEGREE A-V BLOCK

The one subject whose repository tracing showed second degree A-V block with Wenckebach phenomenon was a twenty-three year old pilot who was asymptomatic at the time of his clinical evaluation approximately eight months later (Fig. 19). His history revealed that a few weeks prior to the recording of the repository electrocardiogram he had twice been awakened from sleep by shortness of breath of sufficient severity to require him to remain sitting for the remainder of the night. During the same period he had occasionally noticed fleeting episodes of lightheadedness during physical stress which were

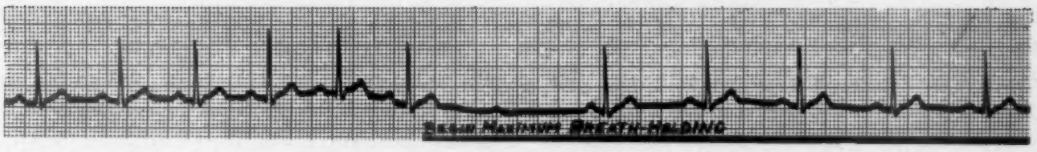


FIG. 20. Electrocardiogram, lead II, in the same subject eight months after the record shown in Figure 19. Blocking of a sinus impulse occurred at the height of the inspiration just prior to breath-holding each time this maneuver was performed.

relieved by sitting down and resting. He was not aware of fever or of other symptoms suggesting systemic illness during this period.

At the time of his evaluation his resting electrocardiogram showed a P-R interval of 0.20 second. On two different occasions, blocking of atrial impulses occurred at the height of inspiration prior to breath-holding but extensive investigation revealed no other abnormality (Fig. 20). It was presumed that myocarditis of unknown etiology had produced transient second degree A-V block.

COMPLETE A-V BLOCK

Complete heart block was present in only one subject, a twenty-seven year old pilot who had completed 2,600 hours of flying without incident. This abnormality was still present at the clinical evaluation eleven months later (Fig. 21). He denied symptoms and stated that his tolerance to exercise was excellent. His past history included scarlet fever, mumps, measles, chicken pox and pertussis in childhood and, during the past several years, recurring bouts of pharyngitis, some of which were apparently due to streptococcic infections. Family history revealed an unknown type of heart disease and diabetes mellitus in his mother, aged fifty-four. Physical examination was within normal limits, showing only moderate obesity and the expected variation in intensity of the first heart sound which was also reduplicated. Results of laboratory and roentgenographic studies were within normal limits.

Complete heart block persisted unchanged throughout various stressful maneuvers. The resting electrocardiogram showed a relatively fast ventricular rate of 58 per minute with an atrial rate of 72 per minute. A double Master test produced an increase of ventricular rate to 70 per minute and of atrial rate to 95 per minute. During treadmill studies with maximum exercise the pulse rate rose to 140 per minute. During these studies relatively high systolic and diastolic blood pressure developed abnormally early in the procedure. Ventilatory volume in relation to work intensity was also increased. These mechanisms apparently compensated for the inadequate cardiac output. No other abnormalities were demonstrated. The relatively normal ventricular rate at rest, 55 to 60 per minute, had apparently prevented recognition of complete heart block until the routine electrocardiogram was obtained.

COMMENTS

Incidence of Prolonged P-R Interval in Normal Subjects: Most authorities place the upper limit of normal A-V conduction time at 0.20 or 0.21 second and occasionally longer in normal subjects. Most agree that prolongation of A-V conduction time beyond 0.20 or 0.21 second occurs rarely enough in normal persons that such values warrant strong suspicion of underlying heart disease. Observations from the present study do not contradict this concept. In an exceptionally large group of subjects without apparent disease and in probably "better than average" health, a prolonged A-V conduction time was found to occur with a frequency of 5.2 per thousand. At this rate, a P-R interval longer than 0.20 second would be encountered once among 200 healthy persons. On the other hand, first degree A-V block has been found in 2 to 3 per cent of hospitalized patients[6,7] and patients with known heart disease.[4,5] Comparing these figures, one might, omitting consideration of other clinical data, anticipate that prolonged A-V conduction time in a given subject would be four to six times more likely to occur as a manifestation of disease than as a normal physiologic variant.

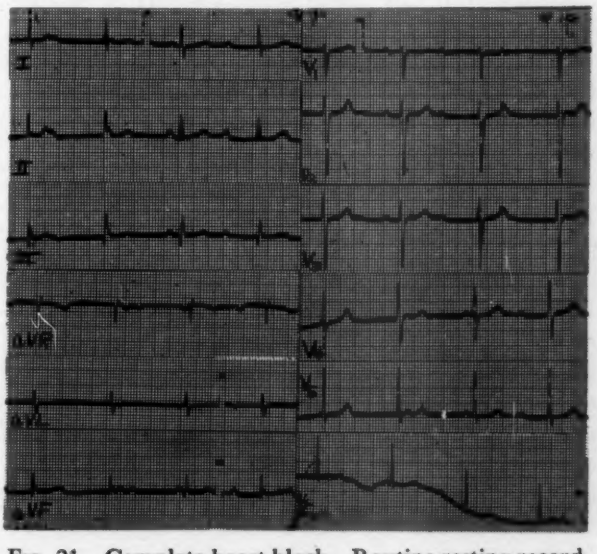


FIG. 21. Complete heart block. Routine resting record.

In such a subject the necessity for a careful search for associated disease is obvious.

While 0.20 or 0.21 second is usually considered the upper limit of normal A-V conduction time, many attempt to define a second higher limit above which A-V conduction time does not exist as a physiologic variant. Thus, it is stated in one text[10] "that although the P-R interval ranges between 0.12 and 0.20 second in adults with cardiac rates between 60 and 80, values up to 0.22 second may be noted in apparently normal hearts." Similarly, another[11] states that the P-R interval may normally be as long as 0.24 second in some subjects. Campbell's observations[5] in a large number of cases of first degree A-V block led him to express the opinion that P-R intervals of 0.26 second or more would not be expected in normal hearts.

Exceptions were noted by Manning[3] whose report of electrocardiographic abnormalities in the absence of heart disease included six apparently normal subjects with a P-R interval of from 0.24 to 0.28 second. Three healthy young subjects with first degree A-V block in the group studied by Graybiel and associates[2,12] had P-R intervals of from 0.25 to 0.28 second. In the present survey seventy of 350 subjects with first degree A-V block (20 per cent) had A-V conduction times exceeding 0.24 second. It is evident that values of this magnitude will occur as normal variants even more rarely than those which are only moderately prolonged. In this respect it may be noted that two, the subject in whom left bundle branch block had developed and the one believed to have coronary disease with anginal pain, of the five with clinical evidence of organic disease had P-R intervals of 0.25 second in their initial repository records. On the other hand, twenty-three others had P-R intervals of 0.25 second or more and were found to have no demonstrable cardiac or other organic disease. The present series provides additional evidence that P-R intervals above 0.24 second and even above 0.30 second may occur in the absence of disease.

These greatly prolonged A-V conduction times should be viewed similarly to other physiologic phenomena, such as height or circumference of the head, which are capable of quantitative measurement, with the more extreme values located farther out on the descending limb of a bell-shaped incidence curve. While the higher values would be found in normal subjects with diminishing frequency, one could not select a point above which abnormality would always be expected. A similar view has been expressed by Jervell[13] who, from observations on a large series of cases of A-V block associated in most instances with disease, concluded that it was impossible to draw any sharp line between physiologic and pathologic values for A-V conduction time.

In this study the population was sufficiently large and homogeneous to permit a valid index of the incidence of first degree A-V block in healthy people. The finding of 350 subjects with prolonged A-V conduction represents an incidence of 5.2 per thousand. This incidence did not appear to be influenced by age. No increase in the incidence of prolonged A-V conduction time was apparent with increasing age as was observed with certain other abnormalities found in the surveyed population for example, right bundle branch block. A greater incidence rate was observed in Negroes, but an occurrence of seven cases of first degree A-V block in a Negro population of 409 did not definitely establish this figure as the true incidence of this abnormality in the Negro race. Neither weight, height, degree of overweight nor cholesterol levels appeared to correlate with the incidence of first degree A-V block.

Effect of Age: While the number of subjects showing prolonged A-V conduction time did not appear to vary appreciably among the different five-year age groups, a difference was apparent when degree of prolongation was considered. The population of 67,375 consisted of nearly equal numbers of subjects below and above thirty years of age, 49.85 per cent below and 50.15 per cent above. There were approximately equal numbers in these two age groups, 143 below thirty and 137 above thirty, who had P-R intervals ranging from 0.21 to 0.24 second. However, P-R intervals of 0.25 second or over were found in forty-five subjects under thirty and in twenty-five over thirty years old. If prolongation of A-V conduction to 0.27 second or more was tabulated, it was found to occur nearly twice as often in those below thirty, the actual numbers of each group showing these values being twenty-five and thirteen. This difference suggests that greatly prolonged A-V conduction times occur more commonly in the younger age groups. A greater degree of vagotonia, thought to be a factor in the bradycardia and sinus arrhythmia seen more commonly in the young, might also

be at least partially responsible for the higher incidence of the longer P-R intervals in younger subjects of the present series.

Effect of Heart Rate: It is generally accepted that the normal P-R interval varies with the R-R interval. The absence of a consistent or direct relation between heart rate and A-V conduction time was noted by Bruenn[14] in his study of impaired A-V conduction due to rheumatic fever. In studies of subjects with normal P-R intervals, neither Savilahti[15] nor Schlamowitz[16] observed a consistent relationship between A-V conduction time and heart rate, despite a widespread impression that the P-R intervals usually shorten with more rapid heart rates. In our series P-R intervals prolonged from slight to marked degrees were seen in association with either relatively fast or slow heart rates with approximately equal frequency. In general, prolongation of the P-R interval was independent of the heart rate. In some subjects the P-R interval varied directly with change in heart rate. In others the P-R interval varied inversely with change in heart rate and some showed very little change in the P-R interval during large changes in heart rate. Conversely, it was not unusual to find marked changes in the P-R interval of some subjects without significant changes in heart rate.

Thus it appeared that the sinus pacemaker and the A-V conducting mechanism reacted independently to vagal inhibitory and sympathetic accelerator influences. This apparent independence was also illustrated by the different times at which changes in heart rate and P-R interval appeared after performing a stressful maneuver. The change in heart rate might appear before or after the occurrence of the induced alteration of P-R interval. A lack of relationship between the P-R interval and sinus rate was exhibited, therefore, by differences in the reaction time as well as in the magnitude and direction of the response.

The inability to describe a consistent relationship between these two parameters of cardiac function is attributable not only to differences between subjects but also to other complex variables which influence these two parameters. For example, the occurrence of a shorter P-R interval during slower heart rates can be explained by assuming that A-V conduction is improved by reason of the longer time available for recovery between periods of activity. During more rapid heart rates the reverse situation might be expected. Furthermore, during rapid heart rate it would not be surprising to find lengthening of the P-R interval if atrial excitation occurred early enough in the cardiac cycle to coincide with the relative refractory period. Shortening of the P-R interval with increases in heart rate can be attributed to increased conductivity resulting from the same sympathetic influences that stimulate the sinus pacemaker. These explanations are plausible and somewhat satisfactory. All are alike in failing to reflect many complex and interrelated changes in cardiac cellular physiology taking place simultaneously as their chemical and electrical environment changes in response to alterations in vagal and sympathetic stimulation, supply and utilization of oxygen, production and transport of metabolites and other complicated metabolic functions. Were our understanding of these alterations and their interrelations complete, the reaction of A-V conduction time would undoubtedly be quite predictable. It is more accurate to report that the changes in A-V conduction time were unpredictable rather than unrelated to heart rate.

Relation of P Wave and P-R Interval: The values for P wave duration generally exceeded those regarded as average, and frequently those considered as the upper limit of normal. The difficulty in setting a definite upper limit of normal for P wave duration is reflected in the relatively large range of 0.10 to 0.12 second usually cited by different authorities as the upper normal limit for this measurement.[4,12,17–22] A survey of the P wave duration in a large representative sampling of the normal records from the population of 67,375 fliers showed values in the normal group which were quite similar to those found in the present group with A-V block.[23]

Values closer to those in the present series were observed by Caceres and Kelser[24] in a recent study which utilized magnified tracings for the determination of P wave duration. These investigators found that forty-four of fifty normal subjects showed a P wave duration of 0.12 second or more in one or more leads. The maximum values seen in any lead, usually aVF and V_5, averaged 0.13 second.

Four of the initial 350 records showing prolonged A-V conduction contained negative P waves in limb leads II, aVF and III, indicating a vector axis between −45 and −75 degrees. Such P waves have usually been regarded as of nodal origin with A-V block causing the P-R interval to be prolonged to over 0.10 second.

The latter condition would imply a high nodal focus. This type of ectopic rhythm has frequently been observed to develop passively in association with vagal inhibition in subjects with normal A-V conduction. In the majority of subjects observed during respiratory maneuvers in this laboratory[25] this apparent change in location of the pacemaker (from the sinus node to a lower focus) occurs with little or no change in the P-R interval. The time from onset of the negative P wave in lead II remains normal and essentially the same as before when the P wave was positive, suggesting that anatomically the shift of location of the pacemaker has not been great. In such subjects with normal P-R intervals, it seems more probable that the inverted P waves in leads II, aVF and III arise from a pacemaker situated in the atrium rather than in the A-V node. Accordingly, the term "atrial rhythm" would more accurately describe this form of ectopic rhythm in which the P-R interval remains normal.

Figure 10 illustrates the development of atrial rhythm in association with defective A-V conduction. In some subjects the initial period of pronounced vagal inhibition after breath-holding is followed by cyclic fluctuations in vagal tone. The latter effect is manifested by marked slowing of heart rate within a few seconds after release of breath-holding followed shortly by several cycles during which heart rate fluctuates, markedly at first but gradually decreasing in magnitude, in phasic fashion. The mechanism is probably that of sinus arrhythmia, increased to a greater degree than usual by the greater depth of respiration and modified by chemical alterations in the blood and hemodynamic changes that result during breath-holding and recovery.

Whatever the mechanism responsible for prolonged A-V conduction in these subjects, its influence persisted for long periods of time despite its apparent lability during short periods of observation. In most of these subjects, first degree block was still present months after its discovery. Although more advanced degrees of A-V block could be induced in some subjects, this cannot be taken to indicate progression of an underlying disorder.

Etiology of Prolonged P-R Intervals: While most of the subjects had no clinically significant cardiac abnormality, the etiology of the conduction defects remained obscure. Like others in the general population, most of these subjects had experienced illnesses in the past which, although seemingly of little consequence, conceivably could have altered A-V conduction. Since the date of onset of prolonged A-V conduction was not known, an etiologic factor could not be established.

In known instances of prolonged A-V block resulting from infections and rheumatic fever, persistence of the block is usually interpreted as evidence of myocarditis with residual structural damage to the conduction system. First degree block associated with rheumatic fever usually returns to normal gradually while that observed during acute infections such as the exanthemata or other viral infections is usually transient. Electrocardiographic studies are rarely performed during such illnesses and there is no factual basis for concluding that permanent A-V block does not occur in certain instances. Assuming myocarditis to be a necessary prerequisite for permanent first degree block following infection, there is ample evidence of its frequency in association with many acute infections of various etiologies.[26] One might postulate that many of these 350 subjects had at some time experienced mild degrees of myocarditis, fortuitously located in the vicinity of the conductive tissues, leaving permanent residual damage which was clinically apparent only by its effect on A-V conduction. Such a concept provides little satisfaction since at present it is capable neither of being proved nor disproved.

Significance of Response to Autonomic Stress Tests: In most of the subjects tested, a greater reduction of the P-R interval was produced by administration of atropine than by either standing or exercise, the mean magnitude of reduction being about one and a half times greater after administration of atropine than after either of the other two measures. The greater potency of atropine in reducing A-V conduction time was also illustrated by comparing the results seen in the ninety-one subjects who were tested by all three measures. The P-R interval decreased to 0.20 second or less in 88 per cent after administration of atropine, in 74 per cent after exercise and in 68 per cent after standing. However, 89 per cent of this same group demonstrated shortening of the P-R limit to 0.20 second or less as a result of both standing and exercise. A combination of these two procedures might produce normal P-R intervals in such subjects as often as administration of atropine, and would in many instances be

attended with less difficulty and inconvenience than the use of atropine.

One of the more striking observations in this group was the marked lability of A-V conduction mechanisms during stress testing such as breathing maneuvers or orthostasis. The greatest change in P-R interval was usually noted in subjects who had the longest P-R interval at rest. Usually those showing marked changes as a result of one procedure also exhibited pronounced responses to other procedures having similar effects on autonomic activity.

Differentiation of Pathologic from Physiologic P-R Interval Prolongation: It is usually inferred that such lability of A-V conduction time reflects excessive vagal activity as a prominent factor in the mechanisms responsible for the delay in A-V conduction. The evidence supporting this concept is largely indirect and derived from observations of the effect of atropine and other agents on the P-R interval. Early studies suggested that the response of the P-R interval to administration of atropine might aid in identifying the etiology of first degree A-V block. This seemed particularly applicable to patients with prolonged A-V conduction in whom rheumatic carditis was a possibility, the assumption being that the production of normal P-R intervals by atropine administration implied absence of this disease. It is now generally recognized that prolonged A-V conduction time associated with various specific disease states is apparently reduced to normal by administration of atropine as readily as in patients in whom no associated disease can be demonstrated.[6,13,14,27,28] Others[3,29–32] have shown similar changes in A-V conduction as a result of standing or exercise.

Efforts have been made to find other agents and procedures which would permit differentiation of the prolonged A-V conduction time due to disease from that of functional origin. The results of one such study[33] suggested that carotid sinus pressure after an injection of ergotamine produced a sufficiently greater lengthening of the P-R interval in patients with rheumatic fever to separate them from healthy subjects with first degree block. The numbers involved were probably too small to furnish conclusive evidence of the value of the test. Lability of the prolonged P-R interval appears to be a nearly constant characteristic of this form of block regardless of its etiology. In addition, such measures sometimes fail to produce significant reduction of a prolonged P-R interval in apparently normal persons. In many studies relatively small subcutaneous injections of atropine have been used so that the question of adequate dosage can also be raised. The inherent lability of A-V conduction in first degree block leads one to doubt that the effect on P-R interval of agents which alter autonomic tone will be successful in differentiating patients with underlying disease.

Associated Cardiac Arrhythmias: In some subjects lability of the cardiac mechanism was also demonstrated by development of arrhythmias. Most of these occurred with stress testing during increased vagal activity. Blocking of sinus impulses, for example, occurred at the height of inspiration prior to breath-holding or following its release. Vagal activity is predominant at both of these stages of the breath-holding maneuver and is manifested usually by cardiac slowing of varying degree. Second degree block with Wenckebach periods also appeared in the period after release of breath-holding. Second degree block with Wenckebach periods, observed in one subject at rest, was replaced by first degree block after exercise, which decreased vagotonia.

A-V dissociation was seen more often during stress procedures at a time when sympathetic tone would be expected to be predominant, as after standing or performing an exercise test. As in normal persons without A-V block it was common to see this arrhythmia after atropine was administered. When it occurred in the presence of A-V block it seemed to differ in that ventricular capture occurred more frequently. P waves commonly appeared on the descending limb of the T wave (Fig. 17).

In a few subjects stress tests induced multiple arrhythmias. In one, for example, atrial premature contractions, atrial rhythm, second degree A-V block with Wenckebach periods, second degree block with a lower atrial pacemaker and nodal escape beats, and A-V dissociation were observed at various times. In two others similar arrhythmias developed during testing procedures. In these the propensity for arrhythmias to develop potentially detrimental to cardiovascular hemodynamics was in itself considered a relative hazard in flying situations, despite absence of demonstrable disease.

Sinus bradycardia and sinus arrhythmia, generally thought to denote relative vagotonia, were often pronounced in these subjects. Among the 139 evaluated, heart rates under basal

conditions obtained prior to exercise were less than 50 per minute in twenty-five subjects. Pronounced degrees of sinus arrhythmia were present in seventeen while at rest, with rates varying rhythmically from around 45 or 50 to 65 or 70 per minute. In addition, in ten other subjects with regular sinus bradycardia at rest marked sinus arrhythmia developed during the period immediately after exercise. The latter phenomenon suggests some delay in achieving a balance between sympathetic acceleration and vagal inhibitory effects during periods when increases of sympathetic tone were achieved. While these manifestations usually attributed to relative vagotonia were impressive in a rather large proportion of the group with A-V block, they did not differ significantly in this respect from other subjects in this survey without A-V conduction disturbances. Therefore, it appeared that these features could not be positively correlated with the prolonged A-V conduction.

Associated Organic Disease: The absence of disease in the majority of the group with first degree block was a consistent and impressive feature. After clinical evaluation of 139 of the original 350 subjects, evidence of organic disease was definite in only four and probable in a fifth. Even in these five, representing about 4 per cent of those evaluated, symptomatic manifestations at the time of examination were minimal or absent. The one subject with mild hypertension and the one with left bundle branch block had always been asymptomatic. The subject with peptic ulcer and the one with diabetes had become asymptomatic after treatment of the acute manifestation. In both, dietary measures were adequate thereafter in providing symptomatic control. The symptoms of the fifth were atypical and objective findings were inconclusive in establishing definitely the presumptive diagnosis of coronary artery disease.

Demonstration of organic disease in a subject with an A-V conduction disturbance does not constitute proof of a common etiology. This platitude seems particularly applicable in the present study since prolongation of A-V conduction time appears to be a particularly nonspecific type of reaction, and since the majority of subjects had no demonstrable disease or other factors which could be definitely related to the conduction defect. It was presumed, however, that in the three subjects with cardiovascular diagnosis and probably the one with diabetes, disease of the coronary vessels was responsible for the prolonged A-V conduction.

In the case of the subject with *duodenal ulcer*, one might postulate excessive vagal tone as the common factor in the etiology of the ulcer and the first degree A-V block. The possibility of such a relation has been commented on previously. If increased vagal tone is often present in patients with peptic ulcer, it would seem reasonable that vagal effects might be manifested also in their cardiovascular reactions. Although attractive as a theory, direct evidence for such a relationship is lacking. In support of the association are the studies of Draper and associates,[34] who attributed the greater than expected frequency of sinus bradycardia and sinus arrhythmia in patients with ulcer to a possibly greater vagotonia. Jervell[13] commented on the frequency of slowed A-V conduction in patients with peptic ulcer after finding thirty-six cases among 317 patients with A-V block, most of whom had organic heart disease. Biorck,[35] in reporting on two patients with peptic ulcer and A-V block, presented evidence for a possible increase in vagal activity as a common factor in both. In the present study a few had past histories suggestive of distress due to ulcer and three had obtained x-ray studies of the gastrointestinal tract which in each instance failed to reveal disease. Thus, only one case of ulcer was actually demonstrated among 139 with prolonged A-V conduction who were clinically studied. This is an unimpressive incidence for a disease as common as peptic ulcer.

The special electrocardiographic studies in the other four subjects with definite organic disease also failed to exhibit any characteristic change in A-V conduction or other signs that separated them from the group without apparent disease. Their responses to postural changes, exercise, breathing maneuvers, carotid massage and administration of atropine were essentially similar to those commonly observed.

Second Degree A-V Block: The only instance of second degree block in the 350 repository tracings also represented the only subject with a history of definite cardiac symptoms. These symptoms were transient and, while disturbing for a time, were not incapacitating, Had this illness been more remote, it is not improbable that it would be forgotten over the years. Thus, had the A-V block been discovered many years later, this subject might also have given a negative history. However, the partial A-V

block was not present on examination eight months later and could not be induced, although single blocked sinus impulses occurred. There seems little doubt that the etiology of the A-V block was due to cardiac involvement, probably myocarditis, associated with a mild infection of unknown etiology. The absence of apparent disease a few months later suggested that residual cardiac damage, if present at all, was mild and probably not clinically significant.

In three other subjects of the 139 examined, second degree A-V block with Wenckebach phenomenon was observed transiently. In each instance it appeared during periods of relative vagotonia. In two of these, the partial block was induced by respiratory maneuvers and was seen only transiently during the period of rebound vagal activity after breathing maneuvers. The same maneuvers after administration of atropine failed to produce this arrhythmia. In the third subject, transitory or intermittent second degree A-V block with Wenckebach phenomena was observed only in a resting tracing taken prior to an exercise test. It was reduced to first degree A-V block after exercise, presumably as a result of sympathetic influences. Neither history nor examination revealed evidence of disease in these three. The possibility of remote cardiac disease, such as myocarditis, exists, but the presence of vagotonia or unusual responses to vagal stimulation seems at least as likely to be the etiology. Similar cases of second degree A-V block without apparent disease have been reported.[29,36,37]

Complete Heart Block: The finding of only one case of complete heart block among the population of 67,375 illustrates its rarity. The surveys of Graybiel[2] and Manning[3] of similar smaller populations did not reveal any subjects with complete heart block. There are a number of other reports of isolated instances of complete heart block without apparent underlying heart disease. Campbell[38,39] commented on the relative frequency of congenital heart block in younger persons in comparison to heart block associated with organic heart disease, estimating that about 50 per cent of cases of complete heart block found in patients below age fifty were of the congenital variety.

His and other reports[40,41] frequently illustrated features which would be unusual in acquired complete heart block. Among these were ventricular rates of 40 to 50 per minute or higher, QRS complexes which were supraventricular in form, absence of symptoms and other evidence of underlying heart disease, and good prognosis for unrestricted activity and normal life span. Associated intraventricular septal defects, while common, often produced no evidence of impaired cardiac function.

The one subject with heart block in our series presented features consistent with congenital block, although all of the criteria mentioned by Yater[42] were not satisfied. This patient closely resembled one reported on in detail by Turner[43] in whom the disease was believed to be of the congenital variety. At rest, the heart rate of the subject from our survey was 58 per minute. Under conditions of mild stress the ventricular rate increased to between 70 and 75 per minute. During more severe physical stress imposed during treadmill studies, the pulse rate was approximately 140 per minute. Unfortunately, electrocardiographic tracings were not taken during exercise so that the accuracy of this observation is open to question and the nature of the cardiac rhythm unknown. The compensatory factors observed during exercise were apparently effective as the subject denied experiencing distress of any kind during physical effort. His flying record appeared to substantiate these claims.

Summary

Observations from the electrocardiographic data of 350 subjects with first degree A-V block and from clinical studies of 139 subjects from this group are presented. First degree A-V block in a large, healthy population occurred at an incidence rate of 5.2 per thousand. A-V conduction time was greater than 0.24 second in 20 per cent of this group, indicating that a precise value which separates the normal from the abnormal A-V conduction time does not exist. Although the significance of the prolonged P-R interval can be determined only by individual clinical evaluation, there is no doubt that the P-R interval can be markedly prolonged in some subjects who are otherwise normal. In the present series only five of 139 were found to have evidence of organic disease.

In the majority of subjects first degree A-V block was still present at the time of clinical evaluation several months after its discovery. Despite its tendency to persist, the prolonged P-R interval exhibited marked lability both spontaneously and during procedures that altered vagal and sympathetic influences.

The effect of administration of atropine, standing and exercise on the A-V conduction

time was compared. In nearly all, the P-R interval could be reduced to normal by one or more of these procedures. Instability of the A-V conduction mechanism was often demonstrable, particularly in those with the longest P-R intervals. Cardiac arrhythmias such as A-V dissociation, blocked sinus impulses, atrial rhythm, nodal escape beats and A-V dissociation could often be induced by stress. In three subjects, transient second degree A-V block with Wenckebach periods appeared either spontaneously or in response to respiratory maneuvers. While these changes could be related to alterations in vagal tone, individual responses were not always predictable and the response of the P-R interval to such alterations frequently seemed independent of the sinus node response.

Observation of one case of second degree A-V block, apparently due to myocarditis, and one case of complete A-V block, presumably congenital, are included.

References

1. Ferguson, D. O. and O'Connell, J. T. Cardiovascular observations: electrocardiograms of men without heart symptoms. *U. S. Navy M. Bull.*, 24: 860, 1926.
2. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1000 young healthy aviatois. *Am. Heart J.*, 27: 524, 1944.
3. Manning, G. W. Electrocardiography in the selection of Royal Canadian Air Force aircrew. *Circulation*, 10: 401, 1954.
4. White, P. D. Heart Disease, 4th ed., p. 933. New York, 1956. The Macmillan Co.
5. Campbell, M. Latent heart block. *Brit. Heart J.*, 5: 163, 1943.
6. Logue, R. B. and Hanson, J. F. Heart block. A study of 100 cases with prolonged P-R interval. *Am. J. M. Sc.*, 207: 765, 1944.
7. Brody, J. I., Golden, L. H. and Tobin, J. L. A review of 3,369 electrocardiograms in young male hospitalized patients. *Am. Heart J.*, 53: 821, 1957.
8. Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
9. White, P. D., Leach, E. C. and Foote, S. A. Errors in measurement of the P-R (P-Q) interval and QRS duration in the electrocardiogram. *Am. Heart J.*, 22: 321, 1941.
10. Friedberg, C. K. Diseases of the Heart, 2nd ed., p. 26. Philadelphia, 1956. W. B. Saunders Co.
11. Barker, J. M. The Unipolar Electrocardiogram. A Clinical Interpretation, p. 454. New York, 1952. Appleton-Century-Crofts, Inc.
12. Packard, J. M., Graettinger, J. S. and Graybiel, A. Analysis of the electrocardiograms obtained from 1000 young healthy aviators. *Circulation*, 10: 384, 1954.
13. Jervell, O. Functional disturbances of the atrioventricular conduction. *Acta med. scandinav.*, 119: 486, 1944.
14. Bruenn, H. G. The mechanism of impaired auriculoventricular conduction in acute rheumatic fever. *Am. Heart J.*, 13: 413, 1937.
15. Savilahti, M. On the normal and the pathological PQ time of the electrocardiogram. *Acta med. scandinav.*, 123: 260, 1945.
16. Schlamowitz, I. An analysis of the time relationships within the cardiac cycle in electrocardiograms of normal men. III. The duration of the P-R interval and its relationship to the cycle length (R-R interval). *Am. Heart J.*, 31: 473, 1946.
17. Kossmann, C. E. The normal electrocardiogram. *Circulation*, 8: 920, 1953.
18. Ashman, R. and Hull, E. Essentials of Electrocardiography, 2nd ed. The Macmillan Co. New York, 1941.
19. Burch, G. E. and Winsor, T. A Primer of Electrocardiography, p. 15. Philadelphia, 1949. Lea & Febiger.
20. Lepeschkin, E. Modern Electrocardiography, vol. 1, p. 233. Baltimore, 1951. Williams & Wilkins Co.
21. Lamb, L. E. Fundamentals of Electrocardiography and Vectorcardiography, p. 47. Springfield, Ill., 1957. Charles C Thomas.
22. Katz, L. N. Electrocardiography, p. 108. Philadelphia, 1946. Lea & Febiger.
23. Hiss, R. G., Lamb, L. E. and Allen, M. F. Electrocardiographic findings in 67,375 asymptomatic subjects. X. Normal values. *Am. J. Cardiol.*, 6: 200, 1960.
24. Caceres, C. A. and Kelser, G. A. Duration of the normal P wave. *Am. J. Cardiol.*, 3: 449, 1959.
25. Lamb, L. E. Unpublished observations.
26. De La Chapelle, C. E. and Kossmann, C. E. Myocarditis. *Circulation*, 10: 747, 1954.
27. Keith, J. D. Over-stimulation of the vagus nerve in rheumatic fever. *Quart. J. Med.*, 7: 29, 1938.
28. Robinson, R. W. Effect of atropine upon the prolongation of the P-R interval found in acute rheumatic fever and certain vagotonic persons. *Am. Heart J.*, 29: 378, 1949.
29. Holmes, J. H. and Weill, D. R., Jr. Incomplete heart block produced by changes in posture. *Am. Heart J.*, 30: 291, 1945.
30. Manning, G. W. and Stewart, C. B. Alteration in PR interval associated with change in posture. *Am. Heart J.*, 30: 109, 1945.
31. Poel, W. Cardiometric studies in children. III. Report of a case of incomplete heart block due to vagal effect. *Arch. Int. Med.*, 69: 1040, 1942.
32. Scherf, D. and Dix, J. H. The effects of posture on A-V conduction. *Am. Heart J.*, 43: 494, 1952.
33. Gubner, R., Szucs, M. and Ungerleider, H. E. Provocative prolongation of P-R interval in rheumatic fever. *Am. J. M. Sc.*, 209: 469, 1945.
34. Draper, G., Bruenn, H. G. and Dupertuis, G. W. Changes in the electrocardiogram as criteria of individual constitution as derived from its physiological panel. *Am. J. M. Sc.*, 194: 514, 1937.
35. Biorck, G., Gohle, D. and Westman, C. Partial A-V block and duodenal ulcer. *Acta med. scandinav.*, 130: 167, 1948.

36. Levy, R. C. Partial heart block due to increased vagal action; a case report. *Arch. Int. Med.*, 12: 1525, 1939.
37. Benedict, R. B. and Evans, J. M. Second degree heart block and Wenckebach phenomenon associated with anxiety. *Am. Heart J.*, 43: 626, 1952.
38. Campbell, M. Congenital complete heart block. *Brit. Heart J.*, 5: 15, 1943.
39. Campbell, M. Complete heart block. *Brit. Heart J.*, 6: 69, 1944.
40. Donoso, E., Braunwald, E., Jick, S. and Grishman, A. Congenital heart block. *Am. J. Med.*, 20: 869, 1956.
41. Rowe, J. C. and White, P. D. Complete heart block: a follow-up study. *Ann. Int. Med.*, 49: 260, 1958.
42. Yater, W. M. Congenital heart block. Review of the literature, report of a case with incomplete heterotaxy; the electrocardiogram in dextrocardia. *Am. J. Dis. Child.*, 38: 112, 1929.
43. Turner, L. B. Asymptomatic congenital complete heart block in an Army Air Force pilot. *Am. Heart J.*, 34: 426, 1947.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

VIII. Non-specific T Wave Changes*

CAPT. ROLAND G. HISS, MC, USAF, CAPT. KEITH H. AVERILL, MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.

San Antonio, Texas

THIS report is an analysis of 581 examples of non-specific T wave changes detected in an electrocardiographic survey of 67,375 healthy men of various ages on flying status with the U. S. Air Force. It is the purpose of this paper to classify these changes, to compare this group with a series of 6,000 randomly selected normal records, to present the correlative medical data obtained from complete evaluation of 226 of these subjects and to indicate some of the physiologic conditions which may induce T wave variations.

T wave changes with certain physiologic maneuvers have been previously noted. Goldberger[1] pointed out T wave variations following carbohydrate ingestion in certain susceptible persons. Wendkos and Logue[2] described T wave changes in persons with neurocirculatory asthenia which were preventable with injection of ergotamine. Mainzer and Krause[3] noted transitory T wave changes in tracings recorded on subjects with anxiety. Wasserburger[4] has recently described changes in the T wave of the precordial leads induced by hyperventilation in Negro patients which he denotes at "latent juvenile pattern." Scherf and Weissberg[5] described leftward shift of the T wave axis with breath-holding, although they thought this finding was caused by a positional shift of the heart. Blom[6] reviewed much of the literature up to 1951 concerning extracardiac causes for electrocardiographic changes and refers to the work of many who have described T wave changes under the following conditions: fear, gunshot startle, psychiatric patients with emotional reactions, cardiovascular neuroses, hyperventilation, hypoglycemia, tachycardia, insulin shock therapy, administration of adrenergic drugs (depressed T waves), parasympathomimetic drugs (elevated T waves), female hormones and psychoses. T wave changes in healthy young subjects caused by orthostasis, breath-holding, hyperventilation and injection of atropine are reported in a study conducted for the Air Force.[7]

Although physiologic variation of the T wave has received fairly wide publication, the frequent appearance of abnormal T waves in the electrocardiogram of patients with serious heart disease has caused many clinicians to ascribe ominous significance to all variations of the T wave regardless of the circumstances. However, when the clinical correlation is vague or absent altogether, T wave changes must be called nonspecific and diagnoses based solely on such changes are unwarranted. It is our intention to point out the incidence in a large healthy male population and general features of nonspecific T wave changes so that they may not be assigned an unjustifiable importance.

MATERIAL AND METHODS

An electrocardiographic survey was performed on asymptomatic healthy men on flying status with the U. S. Air Force in accordance with Air Force requirements. The details of this study have previously been described.[8] It is only necessary to reiterate that all subjects in this survey were in good health to the best of their knowledge, were subjected to annual physical examinations and were receiving close medical support from their flight surgeons. Electrocardiograms recorded for any clinical indication are not included in this study; all tracings were obtained

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

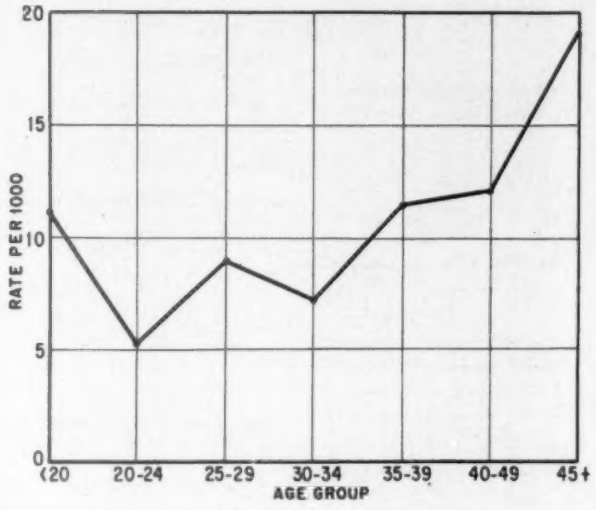


FIG. 1. Rate per thousand subjects in each five-year age group with non-specific T wave changes.

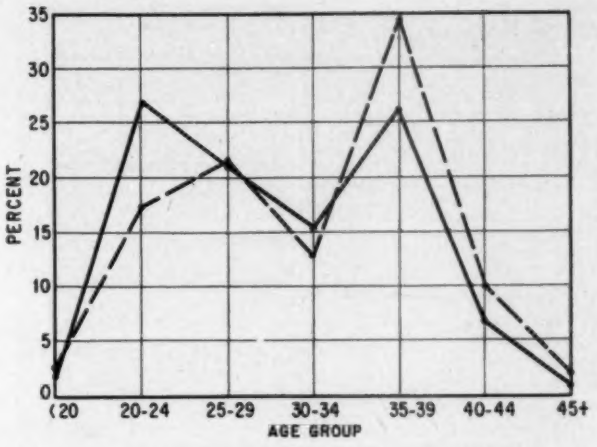


FIG. 2. Percentage distribution by age groups of subjects with non-specific T wave changes (broken line) as compared to the total survey population (solid line). Comparison of the two curves indicates an increase in non-specific T wave changes in the older age group.

only for the purpose of fulfilling requirements of the Air Force regulation.

The types of non-specific T wave changes found in the electrocardiographic survey were categorized. All features of the electrocardiogram as well as the height, weight, body type, heart rate and age of the subjects were entered on IBM cards, compiled and subjected to statistical analysis. The results of this part of the study were compared to a similar evaluation of 6,000 randomly selected normal tracings, 1,000 from each five-year age group of the adult age range represented by the Air Force flying population.

Complete clinical evaluation, including history, physical examination, roentgenogram of the chest, routine laboratory procedures, and determinations of serum cholesterol, phospholipids and fasting blood sugar, was obtained on 226 of the 581 subjects who showed T wave changes. This evaluation also included a routine electrocardiogram recorded with the patient in the fasting state and tracings obtained at full inspiration, during orthostasis and during a routine glucose tolerance test which did not involve blood sampling unless clinically indicated by the metabolic history. Thirty of these evaluations were performed in this laboratory. The others were obtained at the patient's own medical facility through the cooperation of his flight surgeon. Complete evaluation of all subjects with non-specific T wave changes was requested, but only those medical facilities with sufficient time and equipment were able to comply. The 226 subjects who eventually did receive this evaluation thus represent a random selection.

RESULTS

INCIDENCE

Of the 67,375 subjects in the population surveyed, 581 (0.86 per cent) had some type of T wave change in their routine electrocardiogram which necessitated the diagnosis of "abnormal electrocardiogram due to non-specific T wave changes." The rate per thousand incidence of this abnormality expressed by five-year age groups is shown in Figure 1. The higher rate in the first group (less than twenty years of age) is misleading and probably a result of the relatively small number of subjects of this age range in the total population surveyed. The increased rate in the older age groups is undoubtedly a reflection of increased incidence of heart disease in this segment of the population.

Arteriosclerotic heart disease and the early manifestations of left ventricular hypertrophy readily affect the T wave, a point which is well recognized. The error arises in attributing all T wave changes to such etiologies. Figure 2 compares the percentage of subjects with T wave changes in each five-year age group to the percentage distribution of the entire population surveyed.

Of the subjects showing non-specific T wave changes, twenty-one were Negroes (3.62 per cent); this figure is significantly higher than the percentage of Negroes in the entire population surveyed (0.5 per cent).

PATTERNS OF T WAVE CHANGES

The diagnosis of non-specific T wave changes was not made on the basis of a single characteristic configuration, but consisted of a variety of electrocardiographic patterns. All records included in this group demonstrated one or

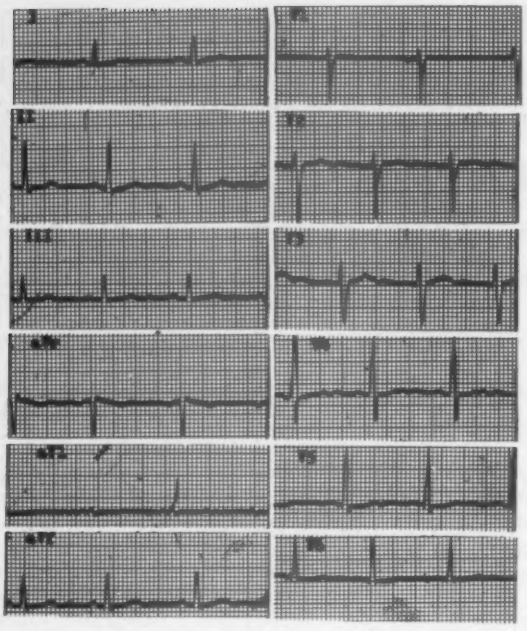


FIG. 3. An example of low T wave amplitude in all twelve leads.

more of the following electrocardiographic findings:

(1) *Low T wave amplitude in all twelve electrocardiographic leads* was observed in 104 (17.9 per cent) of the subjects with non-specific T wave changes. The T wave amplitude in all leads was less than 0.2 mv. (Fig. 3).

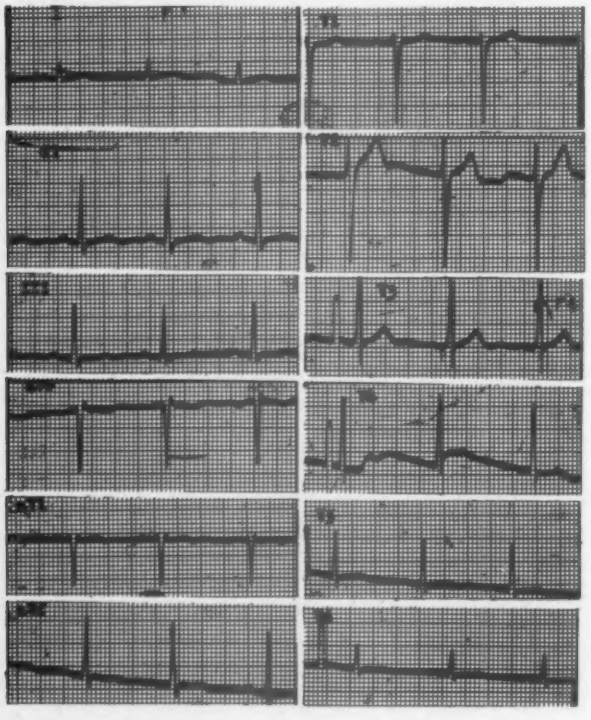


FIG. 4. Low T wave amplitude in the limb and lateral precordial leads.

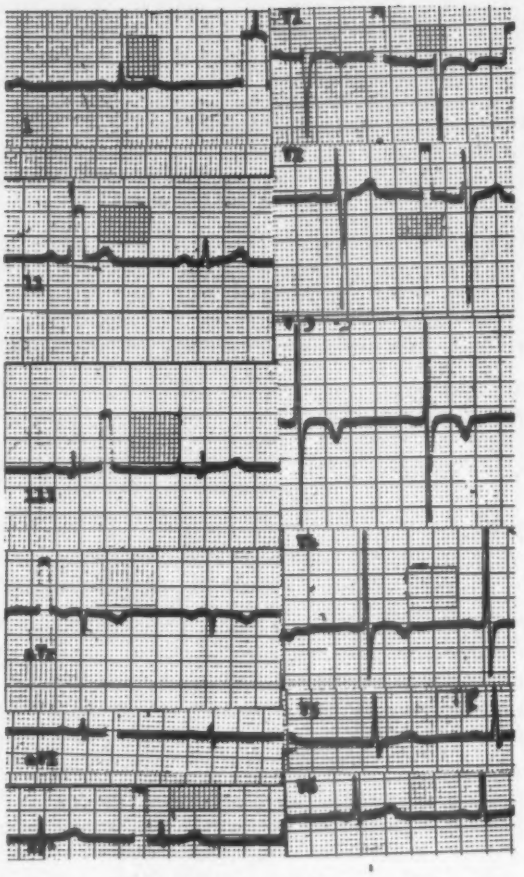


FIG. 5. An example of isolated precordial T wave changes.

(2) *Low T wave amplitude in the six limb leads with normal amplitude in the precordial leads* was seen in twenty-three subjects (3.9 per cent). This relatively rare finding suggests that the majority of the forces of ventricular recovery were in the transverse plane, or that the proximity of the precordial electrodes influenced the character of the T wave.

(3) *Low amplitude or inversion of the T wave in the lateral precordial leads* with normal amplitude in other leads was seen in eleven subjects (1.9 per cent). This phenomenon may be the result of a vertically oriented T axis which would be perpendicular to the lateral precordial leads, or the dampening effect of lung tissue in a person with a wide chest.

(4) *Low amplitude of the T wave in all limb leads plus low amplitude or inversion of the T waves in the lateral precordial leads* was observed in 139 subjects (23.9 per cent) (Fig. 4). This pattern may result from generalized low amplitude of the forces of recovery as in pattern (1)

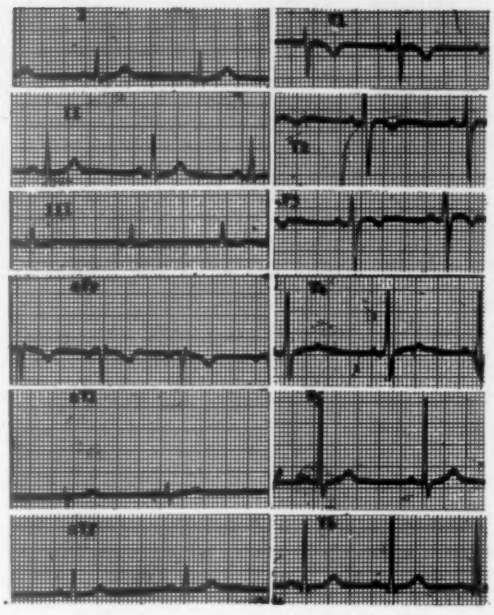


FIG. 6. "Persistent juvenile pattern" of T wave changes.

above, with the proximity of the right precordial leads to the heart producing relatively normal T waves in these leads. In other cases it results from an anteriorly directed T vector which is perpendicular to the frontal plane.

(5) *Isolated T wave changes in the precordial leads* were observed in thirty-four subjects (5.8 per cent) (Fig. 5).

(6) *Inverted T waves in the right precordial leads*, often called the "persistent juvenile pattern," were observed in sixteen subjects (2.7 per cent) (Fig. 6).

(7) *Miscellaneous T wave changes* not fitting into the aforementioned classifications were seen in fifteen subjects (2.6 per cent). Most were tracings demonstrating low T wave amplitude in the precordial leads with normal T waves in the limb leads.

(8) *A wide spatial QRS-T angle* with a leftward T vector and normal T wave amplitude was observed in fifty-five subjects (9.5 per cent) (Fig. 7). In each of these the T vector was zero degrees or less on the standard hexaxial reference system and unassociated with leftward shift of the QRS vector.

(9) *A wide spatial QRS-T angle associated with changes in T wave amplitude* was observed in 233 subjects (40.1 per cent) (Fig. 8).

There were some subjects with two of the described T wave patterns in their tracings. This overlap accounts for the discrepancy between the numbers just listed and the 581 subjects in the series.

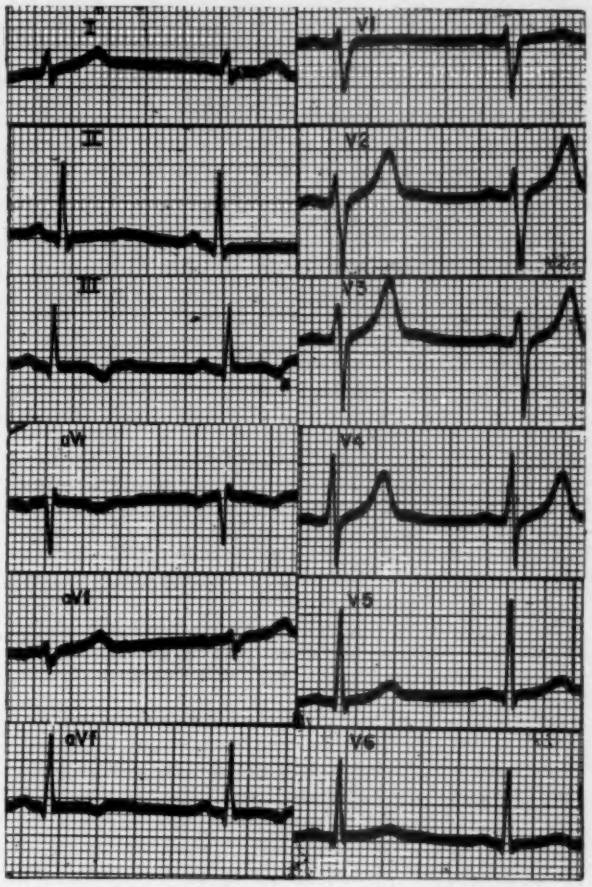


FIG. 7. An example of leftward rotation of the T vector in the frontal plane unassociated with other findings.

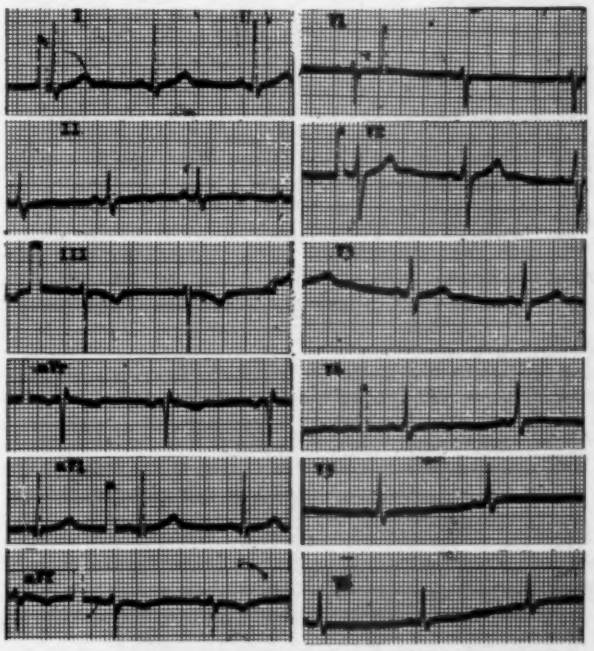


FIG. 8. An example of leftward rotation of the T vector in the frontal plane associated with decreased T wave amplitude in the lateral precordial leads.

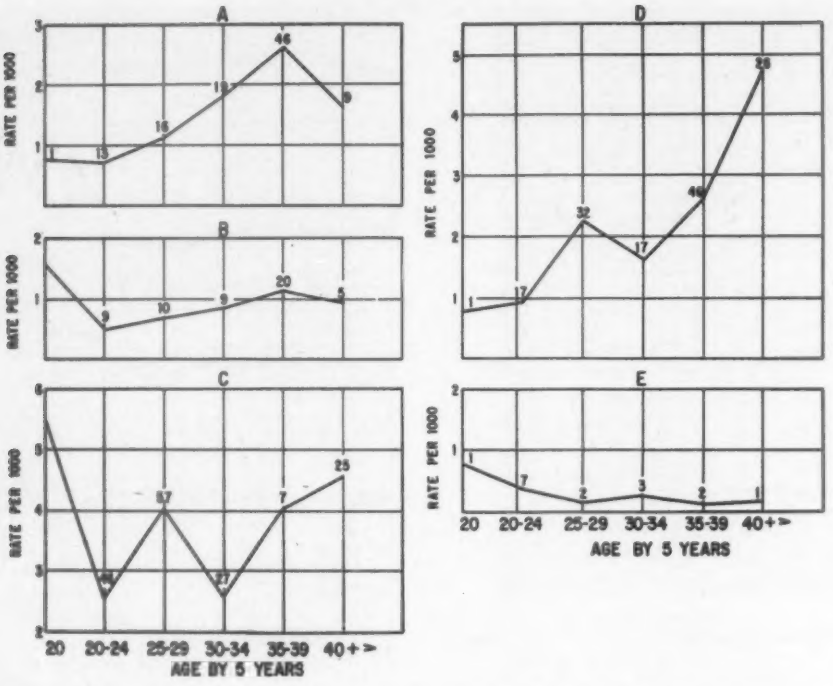


FIG. 9. Age incidence on a rate per thousand basis for the more common patterns of T wave changes. A, low T wave amplitude (less than 0.2 mv.) in all twelve leads. B, leftward rotation of the T vector (beyond zero degrees) unassociated with other findings. C, leftward rotation of the T vector associated with decreased amplitude of the T waves. D, low amplitude T waves in the limb and lateral precordial leads. E, "persistent juvenile pattern." The numbers above the graph at each age group refer to the number of subjects on which this rate was based.

Correlation of Age and T Wave Patterns: The age incidence of each of the T wave patterns was calculated on a rate per thousand basis (Fig. 9). The three curves for the patterns of low T wave amplitude in the limb leads, isolated precordial changes and low T wave amplitude only in the lateral precordial leads have been omitted as there was no variation between age groups for these patterns.

Inspection of the age incidence graph indicates that the pattern of low T wave amplitude in both the limb and lateral precordial leads without widening of the QRS-T angle increases significantly with age. If true, this pattern of T wave change may be given more importance as an indication of underlying heart disease. Follow-up studies will be necessary.

It is of interest to note that the "latent juvenile pattern" is not restricted to the younger age groups and actually has a relatively even age distribution.

Clinical Correlations: An attempt was made to correlate the T wave pattern observed with many factors, including height, weight, race, heart rate, body type, past medical history, family history and laboratory data. Such correlation was essentially inconclusive, with the exception of two impressions. The first of these was that isolated precordial T wave changes were frequently found in electrocardiograms obtained from Negro subjects, and second, that generalized low amplitude T waves in all twelve routine leads were often observed in an obese subject. The distribution of T wave pattern with other data obtained on the entire group was random.

COMPARISON WITH THE NORMAL VALUES SERIES

The frequency distribution of height, weight, heart rate, body type and all commonly recognized electrocardiographic features of the 581 cases of non-specific T wave changes were compared to similar statistics obtained from a detailed analysis of 6,000 normal electrocardiograms, 1,000 for each five-year age group in the adult population. The details will be presented in a subsequent report.[9]

Height and Weight: There was no significant difference in the distribution of height in the group with T wave changes as compared with the

normal group. However, the weights of the subjects showing non-specific T wave changes ranged from 120 to 236 pounds and averaged approximately 6 pounds heavier in each age group than the group with normal values. The influence of weight on the body type (relative obesity) was even more striking. All subjects in both series were classified into one of five basic body types based on standard height-weight tables as follows: group 1, standard weight minus 20 pounds or more; group 2, standard weight minus 10 to 19 pounds; group 3, standard weight plus or minus 9 pounds; group 4, standard weight plus 10 to 20 pounds; and group 5, standard weight plus 20 pounds or more. Standard weights were calculated on the basis of height using the twenty-six to thirty-year age group on the height-weight table of Air Force Manual 160–1.[10]

Fifty-two per cent of the subjects with non-specific T wave changes were 20 pounds or more overweight for the height as compared to 31.6 per cent of those with normal values. This general relationship was found at each age group and was not restricted to the older population. The percentage of overweight subjects became higher in both the normal and abnormal series with increasing age, but the ratio was the same at each five-year age group.

The influence of excess weight as a factor in non-specific T wave changes has been demonstrated several times in this laboratory. We have evaluated markedly obese subjects who showed generalized non-specific T wave changes and borderline positive double Master exercise tests. On successful completion of an appropriate weight reduction program, a normal electrocardiogram and Master test were obtained.

Heart Rate: Heart rates approximated 6 to 7 beats per minute faster for the tracings showing non-specific T wave changes as compared to the group with normal values. This is undoubtedly a reflection of a phenomenon which will be discussed in the part of this paper dealing with T wave changes with relative tachycardia.

T Wave Axis and Amplitude: An analysis of the T wave vector in the frontal plane as well as the T wave amplitude in leads I, aVF, V_2 and V_6 either individually or as combinations of leads in the same plane reflected our criteria for the diagnosis of "nonspecific T wave changes." The median T axis for those with normal values was +45 degrees, whereas the median T axis for the group with non-specific T wave changes was zero degrees. This finding resulted from inclusion of many tracings in which the T wave abnormality was marked leftward rotation of the T axis in the frontal plane. T wave amplitudes in the group with non-specific T wave changes were one-half to one-third of corresponding values and distributions in the group with normal values, as expected. The sum of the T wave amplitude in leads I + aVF (ventricular recovery forces in the frontal plane) was approximately one-half of that in the group with normal values. The sum of the T wave amplitudes in leads I + aVF in the group with non-specific T wave changes was 0.2 mv. (low amplitude) or less in 71 per cent of the subjects as compared to 15 per cent of subjects in the corresponding group with normal values. Similar results were obtained when the sums of the T wave amplitudes in leads I + aVF + V_2 or V_2 + V_6 were compared. The sum of the T wave amplitude in leads I + aVF + V_2 was 0.6 mv. or less in 49.1 per cent of the non-specific T wave tracings as compared to only 9.2 per cent of the group with normal values. The sum of leads V_2 + V_6 of the group with the abnormality was 0.6 mv. or less in 72.1 per cent of subjects as compared to 20.8 per cent in the normal population.

The particular leads were used in measurements of amplitude as they most nearly represented mutually perpendicular coordinates. These measurements will be discussed in detail in a subsequent publication.[9]

QRS Changes: A comparison of the incidence of Q waves in the standard limb leads of 0.03 second or greater did not show any increased incidence in the group with non-specific T wave changes as compared to the group with normal values. This analysis was conducted to determine whether any other evidence of previous myocardial infarction might be suspected electrocardiographically to a greater degree in the group with non-specific T wave changes than in the normal group.

Comparisons of other electrocardiographic features such as QRS amplitudes in leads I, aVF, V_2 and V_6 either individually or as sums of amplitudes in leads in the same plane did not show any significant difference between the group with non-specific T wave changes and those with normal values. This point is important as it suggests that the non-specific diminution of the T wave amplitude was not merely a

TABLE I
Positive Clinical Findings in an Evaluation of 226 Subjects

Finding	No.
History of symptoms possibly suggestive of cardiovascular disease	10
Past medical history	
Scarlet fever	14
Pericarditis	6
Rheumatic fever	5
Poliomyelitis	3
Diabetes	2
Coccidioidomycosis	2
Gout	2
Pyelonephritis	2
Family history	
Myocardial infarction in an older member	10
Arteriosclerotic heart disease without myocardial infarction	9
Hypertension	8
Myocardial infarction in a young member	7
Rheumatic fever	2
Diabetes	1
Physical findings	
Increased blood pressure	7
Pectus excavatum	4
Cardiac murmurs	3
Roentgenographic findings	
Suggestive of old pleuritis	4
Suggestive of old pericarditis	2
Enlarged hilar lymphadenopathy	1

coincidental finding associated with decreased QRS voltage caused by such factors as body weight. Also, if T wave changes of the type described are considered evidence of myocardial disease, one might expect that QRS voltage would be similarly affected. This was not the case in this study. QRS duration, P-R interval, Q-T interval, P wave amplitude, duration and axis, non-specific S-T segment elevation, and rightward terminal QRS forces were found in approximately the same distribution in the group with non-specific T wave changes as compared to the normal group.

TABLE II
Clinical Estimation of Body Habitus

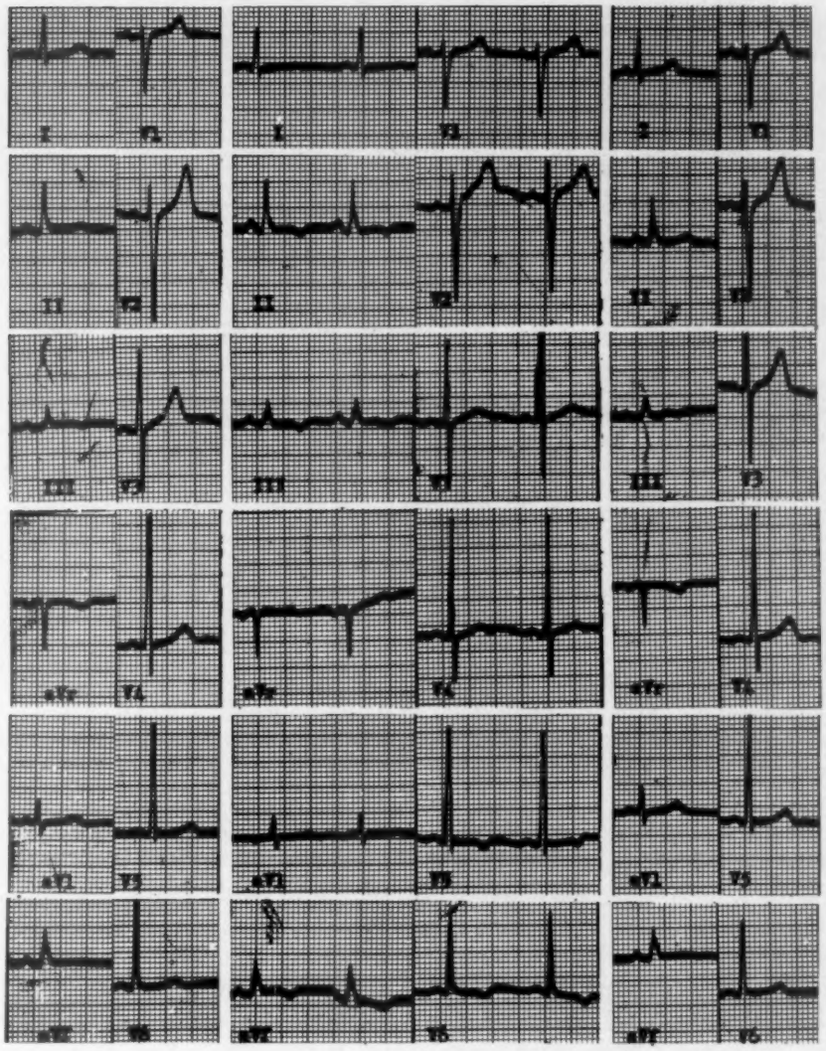
Status	No.
Normal	145
Obese	41
Slightly obese	24
Asthenic	8

CLINICAL CORRELATION AND SPECIAL ELECTROCARDIOGRAPHIC STUDIES

Clinical Evaluations: Of the 581 subjects whose routine electrocardiogram showed non-specific T wave changes, 226 received full clinical evaluation of this abnormality. The past medical history, family history, system review, physical examination, roentgenogram of the chest, routine laboratory procedures, and determinations of fasting blood sugar, serum cholesterol and phospholipids did not reveal any remarkable finding which might not be expected in a similar evaluation of 226 subjects of the same age with normal electrocardiograms. Positive features of these clinical data are tabulated in Table I. The clinical estimation of the body type by the examining physician not based on height-weight tables was obtained in 218 of the 226 subjects (Table II). Table III gives the composite cholesterol values by age group.

TABLE III
Cholesterol Values
Number of Subjects with Various Serum Cholesterol Levels

Total Serum Cholesterol (mg. per cent)	Age by Five-Year Group					Total	Per Cent
	20–24	25–29	30–34	35–39	40 and over		
125–150	2	3	1	4	0	10	5
151–175	4	3	3	6	3	19	9
176–200	11	8	4	12	1	36	17
201–225	2	9	11	11	1	34	16
226–250	4	9	5	15	8	41	19
251–275	3	7	6	10	5	31	15
276–300	1	0	3	12	4	20	9
301–325	0	1	3	4	5	13	6
326–350	1	2	0	5	0	8	4



A B C

FIG. 10. Electrocardiograms of a twenty-four year old subject showing the effect of 100 gm. of glucose in solution administered orally. A, fasting tracing. B, one hour after ingestion of glucose in solution. C, three hours after glucose administration with a return to normal T wave configuration.

Effect of Fasting and Ingestion of Glucose: Of the 226 subjects, 121 (53.5 per cent) had normal tracings when these were repeated in the fasting state. Of these, eighty-eight (73 per cent) showed T wave changes following the ingestion of 100 gm. of glucose in solution (Fig. 10) which in sixty-three subjects (52 per cent) precisely reduplicated the original T wave abnormality. There were an additional fifty-six subjects (24.7 per cent) whose fasting electrocardiograms were still abnormal, but markedly improved from the original tracing; of these, forty-five (80 per cent) showed further T wave changes following oral ingestion of glucose, twenty-six (46 per cent) reduplicating their original electrocardiogram. There were forty-nine subjects (21.7 per cent) whose electrocardiogram was unchanged in the fasting state.

The age incidence of those subjects whose fasting tracings were normal was compared to subjects whose tracings were still abnormal in the fasting state (Fig. 11). In the relatively young age groups there is a slight predominance of subjects whose T wave abnormality disappears in fasting tracings as compared to those subjects with more fixed T wave changes, but in the older age groups the reverse is true. Our reasoning in constructing this graph was to see if T wave lability following ingestion of glucose might be a precursor in the younger subject of more rigid T wave changes at an older age. This may be true, but it is our im-

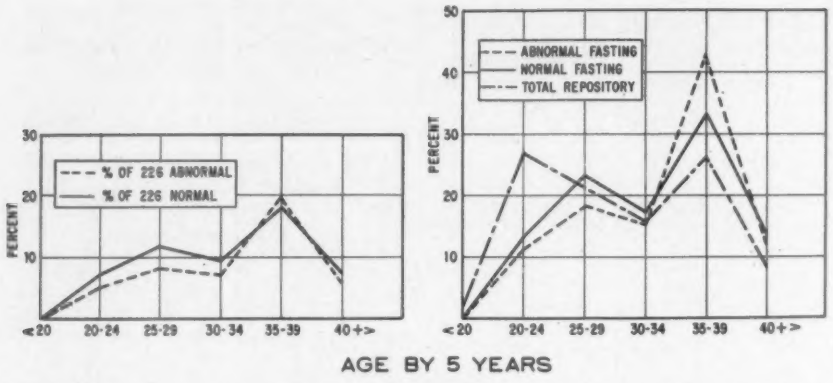


FIG. 11. T wave changes from the original survey which could be attributed to recent ingestion of a meal. The graph on the left compares the subjects at each age group whose fasting tracing was normal with those whose fasting tracing was still abnormal. This information was available for the 226 subjects who received full evaluation. The graph on the right compares the percentage distribution by age group of the subjects with fasting normal tracings but T wave changes following glucose (solid line), and those with T wave changes in the fasting state (broken line), with the percentage distribution by age of the entire survey population.

pression that the proportional figures at each age group are too similar for such a conclusion, particularly since both curves are strongly affected by the relative size of the entire survey population at each age group.

Body Position: Of the 121 subjects whose fasting tracings were normal, seventy-eight (64 per cent) showed T wave changes when an electrocardiogram was recorded in the orthostatic position, with the subjects in the fasting state. Of these, forty-two (35 per cent) precisely reduplicated their original abnormality with orthostasis. Similarly, there were forty subjects of the fifty-six whose tracings were improved, but not entirely normal in the fasting state, who showed further changes with orthostasis, twenty-three reduplicating the original abnormality. Of those subjects whose tracings were completely unchanged in the fasting state, several showed further changes with both ingestion of glucose and orthostasis producing T wave changes of even more striking characteristics.

Deep Inspiration: T wave changes occurred with the subject at full inspiration in thirty-one subjects whose fasting tracings were normal and in eighteen subjects whose fasting tracings were improved, but not normal. In almost all cases where a change of the T wave pattern occurred with deep inspiration, orthostasis or ingestion of glucose, this change was of the same general type that had been noted on the original survey electrocardiogram. This fact suggests that the type of T wave variation in a susceptible subject is not specific for the physiologic maneuver which elicited the change but rather peculiar to that subject. Ingestion of glucose and orthostasis were particularly closely allied in this regard (Fig. 12).

Tachycardia: There were twenty-five subjects (11 per cent) in whom increased heart rate was implicated as the probable cause for the T wave changes (Fig. 13). Repeat tracings under basal conditions were normal (heart rate much slower) and the original abnormality was reduplicated when the rate was increased by orthostasis. The basic mechanism for T wave changes with increased rate or with orthostasis is probably increased sympathetic tone, which is undoubtedly the mechanisms for "anxiety T waves" that others have noted.[3]

Obesity: Although it is thought that marked obesity can be associated with non-specific T wave changes, obesity did not always preclude normal tracings in the fasting state and positive glucose and orthostatic responses were noted in obese subjects in approximately the same frequency as those whose weight was normal. Likewise, there was no uniform pattern by which the Negro subjects responded; half of those evaluated had normal fasting tracings with positive responses to orthostasis and ingestion of glucose and the other half were unchanged in the fasting state.

COMMENTS

It was our impression from this study that for most of the subjects who demonstrated a

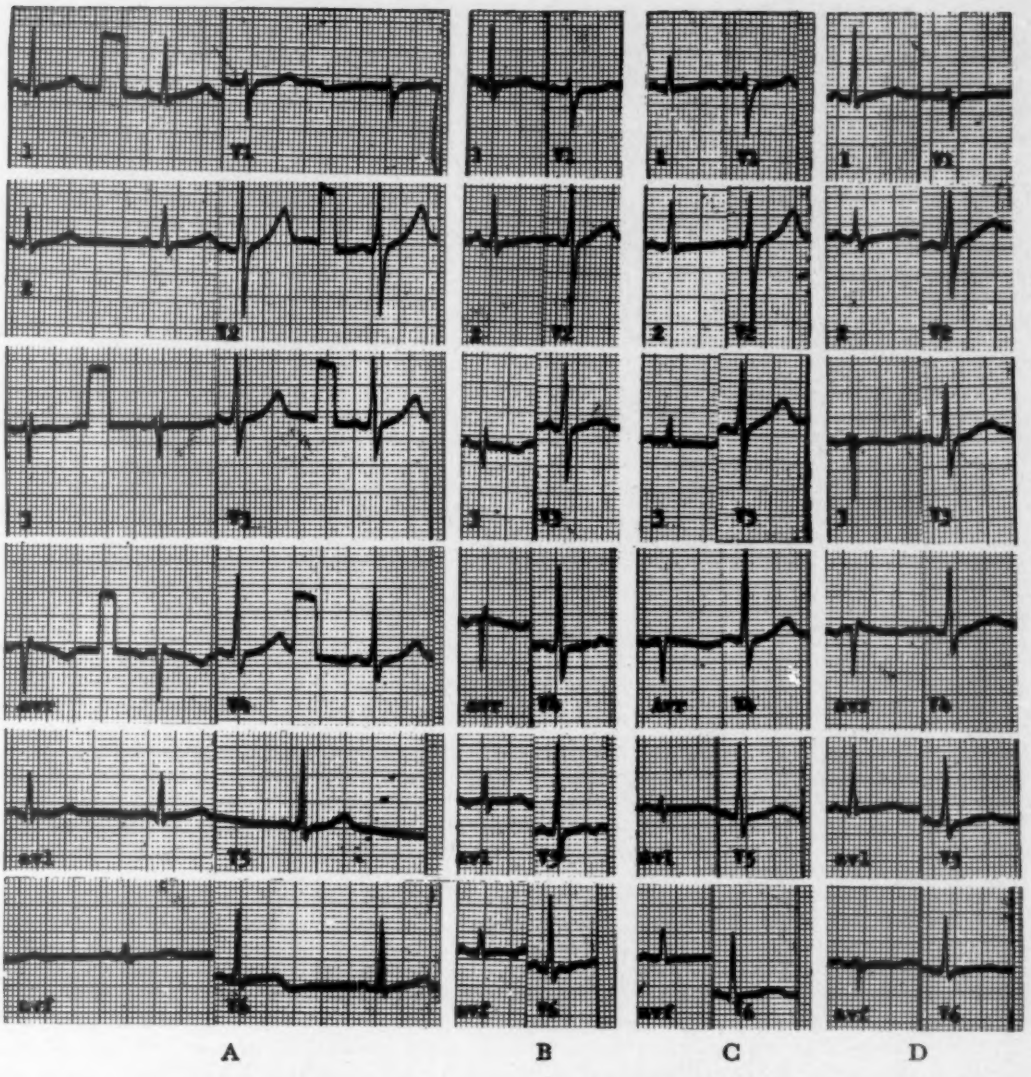


FIG. 12. A series of tracings on a twenty-seven year old subject during various maneuvers. A, subject fasting and recumbent. B, one minute after assuming the upright position. C, at the height of deep inspiration with the subject recumbent. D, one-half hour following ingestion of 100 gm. of glucose in solution. Note the similarity of the effect of orthostasis and ingestion of glucose on the T wave changes.

form of non-specific T wave change in their routine electrocardiogram there was not sufficient evidence to warrant a diagnosis of organic heart disease. The clinical appearance of these men and their evaluation utilizing the common diagnostic parameters employed in cardiovascular investigation did not reveal any feature which would characterize this group or set it apart from completely normal persons of the same age. Body weight and slightly increased heart rate might be the only exception to this. The T wave changes were relatively isolated phenomena in an otherwise healthy picture. The lability of the T wave changes noted with simple physiologic maneuvers indicated that the majority of the original electrocardiographic abnormalities could be attributed to a peculiar idiosyncrasy which is of academic interest, but may not be of diagnostic importance. It should be pointed out, however, by way of caution, that an abnormal T wave fostered by significant disease may show further variation with physiologic maneuver. Demonstration of the lability of a T wave which is abnormal under basal conditions does not prove the innocuous nature of this finding.

There is considerable room for speculation concerning the mechanisms responsible for the T wave changes described. The role of the potassium ion in T wave changes asso-

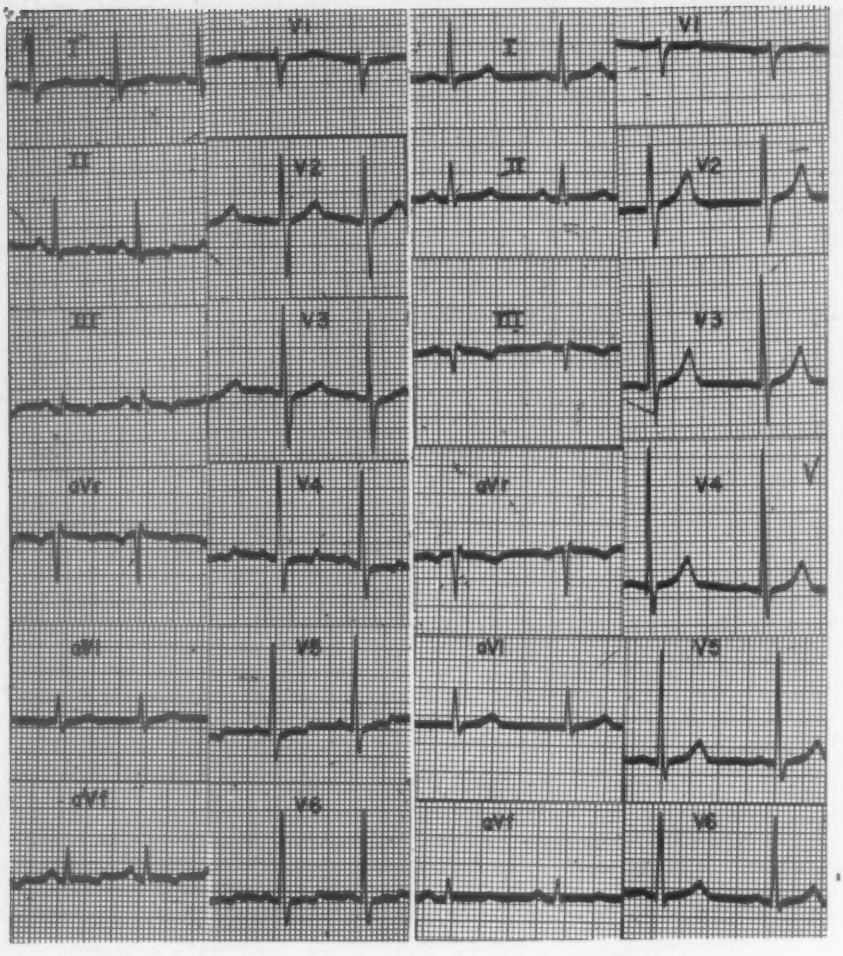


FIG. 13. The effect of increased heart rate and/or anxiety on the T waves of a thirty-three year old officer. A, tracing recorded when he was apprehensive about the outcome of the examination. B, tracing recorded under more basal conditions.

ciated with ingestion of glucose is undoubtedly important, and the role of autonomic tone, both sympathetic and parasympathetic, cannot be overlooked. Other factors probably contribute to the general picture of T wave lability, including intrathoracic hemodynamics, peripheral blood flow and metabolic activity. The mechanics and interrelations require considerably more investigation before they may be fully comprehended.

Many workers have been suspicious of T wave changes seen in routine electrocardiography. Most of these studies, however, have been conducted on populations considerably older than ours in which the incidence of heart disease would be expected to be higher. It is readily admitted that "non-specific" is not synonymous with "innocuous" and diseased hearts may indeed show non-specific T wave changes, but we believe that many of the non-specific T wave abnormalities found in this electrocardiographic survey represent another kind of T wave change, a category which does not usually confront the clinician in practice. These are physiologic T wave changes which are not associated with heart disease so that the subject remains asymptomatic and does not seek medical attention.

The problem is one of separating those T wave changes which are secondary to disease from those which are not. The increase of non-specific T wave changes with advancing age documents the potentially serious nature that abnormal T waves may have; on the other hand, demonstration of grossly abnormal T waves produced by a benign mechanism such as carbohydrate ingestion or orthostasis suggests that physiologic mechanisms must be seriously

considered before making a diagnosis. A longitudinal program on our series will be conducted to attempt delineation of this problem. Pending further studies, however, it is our conclusion that to place ominous significance on isolated T wave changes in a routine electrocardiogram without thorough consideration of the physiologic factors that may be operative would be overreading the tracing and an injustice to the patient.

Summary

An electrocardiographic analysis of 67,375 asymptomatic healthy men on flying status with the U. S. Air Force has revealed the presence of 581 subjects with non-specific T wave changes in their routine electrocardiogram. Complete clinical evaluation of 226 subjects failed to reveal any increase of heart disease or family history of heart disease over what might be expected from a similar analysis of randomly selected men from the same population with normal electrocardiograms.

The types of T wave changes were categorized into nine basic patterns. An attempt to correlate these patterns with any characteristic of the subject or other features of his electrocardiogram was unrevealing.

Comparison of the group with non-specific T wave changes with a series of 6,000 normal electrocardiograms (1,000 from each five-year age group of the adult population) revealed many striking differences. The body weights and heart rates of the group with the abnormality were slightly higher than in those with normal values, and the percentage of overweight subjects in each age group was markedly larger. The T wave amplitude in leads I, aVF, V_2 and V_6 was approximately half that of comparable values in the normal series when each lead was compared separately and when sums of leads in the same plane were compared.

There was an increase in the incidence of non-specific T wave changes in the older age groups. This is likely due to increased cardiac disease expected at these ages.

A complete clinical evaluation was conducted on 226 of the 581 subjects with non-specific T wave changes. There were 121 (53.3 per cent) subjects whose fasting tracing was normal in all respects. In these, T wave changes were often artificially induced following ingestion of 100 gm. of glucose in solution, following orthostasis and with deep inspiration. These T wave changes mimicked the original abnormality seen on the routine survey electrocardiogram.

Obesity was a factor in the production of non-specific T wave changes in several subjects, but the presence of obesity did not preclude normal fasting electrocardiograms.

There were twenty-five subjects, whose T wave abnormality was attributed to increased heart rate and/or anxiety.

Because of the extreme T wave changes which are possible in susceptible subjects under such benign conditions as the postprandial state, respiration or minor anxiety, it is believed that T wave changes found in any routine electrocardiogram should be carefully considered as potentially physiologic. A diagnosis of heart disease on the basis of isolated T wave changes in the absence of clinical correlation or other more specific electrocardiographic findings is not justified.

References

1. Goldberger, E. Unipolar Electrocardiography, 3rd ed., p. 161. Philadelphia, 1953. Lea & Febiger.
2. Wendkos, M. H. and Logue, R. B. Unstable T-waves in leads II and III in persons with neurocirculatory asthenia. *Am. Heart J.*, 31: 711, 1946.
3. Mainzer, F. and Krause, M. The influence of fear on the electrocardiogram. *Brit. Heart J.*, 2: 221, 1940.
4. Wasserburger, R. H. The riddle of the labile T wave. *Am. J. Cardiol.*, 2: 179, 1958.
5. Scherf, D. and Weissberg, J. The alteration of the T-wave by a change of posture. *Am. J. M. Sc.*, 201: 693, 1941.
6. Blom, G. E. A review of electrocardiographic changes in emotional states. *J. Nerv. & Ment. Dis.*, 113: 283, 1951.
7. Hiss, R. G., Smith, G. B. and Lamb, L. E. Pitfalls in interpreting electrocardiographic changes occurring while monitoring stress procedures. *Aerospace M. J.*, 31:9, 1960.
8. Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
9. Hiss, R. G., Lamb, L. E. and Allen, M. F. Electrocardiographic findings in 67,375 asymptomatic subjects. X. Normal values. *Am. J. Cardiol.*, 6: 200, 1960.
10. Air Force Manual 160-1, Medical Examination. April 30, 1953, p. 96.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

IX. Myocardial Infarction*

MAJ. GEORGE B. SMITH, JR., MC, USAF *and* LAWRENCE E. LAMB, M.D., F.A.C.C.
San Antonio, Texas

UNTIL recent years, many physicians considered arteriosclerotic heart disease with myocardial infarction a disease of advancing years, occurring uncommonly before the age of forty. In addition, since Herrick's description of the clinical syndrome,[1] pain has been considered a cardinal symptom in establishing the diagnosis of myocardial infarction.

Studies such as those of Glendy, Levine and White,[2] French and Dock[3] and the more extensive series reported by Yater et al.[4] have demonstrated that arteriosclerotic heart disease occurs in young persons and, not infrequently, causes death through infarction of the myocardium. It is also increasingly evident that myocardial infarction is not always heralded by characteristic pain or any other unique symptoms.

Since myocardial infarction occurs in the younger age groups without characteristic or recognizable symptoms, it presents a particularly difficult diagnostic problem in persons who fly. The effects of an impaired coronary circulation (due to arteriosclerosis) and impaired oxygenation of the blood (due to the hypoxia of altitude) are cumulative. Hypoxemia that might be inconsequential in its effects on a normal heart could cause acute damage to the myocardium with a blood supply compromised by arteriosclerosis. Similarly, coronary circulation might be just adequate to supply the myocardium at ground level, but prove insufficient under the stresses of altitude.

MATERIAL AND METHODS

In April 1957, the U. S. Air Force established the Electrocardiographic Repository at the School of Aviation Medicine. Initial records for this repository were obtained by requiring that baseline electrocardiograms be taken on all rated personnel (pilots, navigators and flight surgeons) at the time of their next annual physical examination, regardless of age. Electrocardiograms are also required on all future selectees for flying training and for the U. S. Air Force Academy. These records and all those which might be taken for other reasons (for example, pressure suit indoctrination or hospitalization) are forwarded to the repository for interpretation and comparison with any previous records. A previous Air Force requirement for annual electrocardiograms on all personnel after age forty was not changed.

These requirements have resulted in the accumulation, interpretation and statistical evaluation of 67,375 electrocardiographic records. The general details of the electrocardiographic survey have been previously reported.[5]

During the initial evaluation of these records, and before any rigid criteria were established, the records of 129 subjects were selected as being compatible with myocardial infarction. Of these, seventy-three were considered compatible with infarction of the inferior wall (diaphragmatic), thirty-five with infarction of the anterior myocardial wall and twenty-three demonstrated other manifestations strongly suggestive of myocardial infarction. Later, more rigid criteria were established for considering electrocardiograms to be compatible with previous infarction.

Criteria for Diagnosis of Myocardial Infarction: These criteria are as follows:

Inferior wall infarction: (1) Q_3 of at least 0.04 second in duration, and followed by an R wave; (2) Q in lead aVF of at least 0.02 second in duration; (3) Q_2 must be present; (4) the amplitude of the QRS complex in lead III must be at least 5 mm. (0.5 mv.), unless Q_3 is greater than 2.5 mm. (0.25 mv.); (5) P_3 must be upright, and there must be an iso-

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

TABLE I

Results of Applying Rigid Criteria to 129 Electrocardiograms Suggestive of Myocardial Infarction

Criteria	No.
Do not meet criteria of infarction	63
Borderline, suggestive of inferior infarction	16*
Borderline, suggestive of anterior infarction	15†
Compatible with infarction of the inferior wall	24
Compatible with infarction of the anterior wall	9
Compatible with infarction of the lateral or anterolateral wall	1
Compatible with infarction of the anterior-inferior wall	1

* These records meet all criteria of inferior infarction, except that P_3 is diphasic or inverted.

† These records meet the criteria of anterior infarction, except that R waves are absent in leads V_1 and V_2, but present in lead V_3.

electric interval between the P and Q waves; and (6) intraventricular conduction must be essentially normal.

Anterior wall infarction: (1) R waves must be absent in leads V_1, V_2 and V_3, *or* there must be a significant localized loss of R wave amplitude in leads V_2, V_3 or V_4; and (2) P waves must be upright in lead V_2.

Of the group of 129 persons originally thought to have abnormal records, fifty-one have had complete clinical evaluation, most of which have included vectorcardiograms. (A large number of the remaining group have had varying evaluations at their bases or elsewhere. These examinations have often been prompted by letters reporting the interpretation of the subject's electrocardiogram at the Electrocardiographic Repository. However, the results of these examinations are frequently placed in personal medical records and are not available to the School of Aviation Medicine.)

RESULTS

When the original records of the 129 subjects were reviewed in terms of the more rigid criteria above, they were reclassified as shown in Table I.

Table II illustrates the relation between the interpretation of the original electrocardiogram and the results of clinical evaluation of fifty-one of these subjects.

Considerable effort was expended evaluating persons whose electrocardiograms did not meet the criteria for myocardial infarction. This was carried out because it is probably not possible to formulate criteria which will entirely differentiate the electrocardiograms of

TABLE II

Interpretation of Original Electrocardiograms and Results of Clinical Evaluation for Fifty Persons

Interpretation	No. First Suspected	No. Seen	"Normal"*	Inferior Infarction	Anterior Infarction
Do not meet criteria	63	18	16	2	...
Borderline, inferior	16	5	4	1	...
Borderline, anterior	15	2	1	...	1
Compatible with inferior infarction	24	17	12	5	...
Compatible with anterior infarction	9	8	1	...	7
Compatible with anterolateral infarction	1	1	...	...	1
Compatible with anterior-inferior infarction	1	...	...	...	...
Totals	129	51	34	8	9

* No clinical or laboratory evidence of myocardial infarction. Abnormal electrocardiograms were considered as electrical variants without clinical significance.

persons who have had myocardial infarctions from those of persons who have not. Two of the eighteen persons whose electrocardiograms did not meet criteria were found to have clinical evidence of myocardial infarction. Conversely, thirteen of twenty-four persons whose electrocardiograms did meet the criteria of infarction were found to have no other clinical or laboratory evidence of myocardial infarction.

In addition to the aforementioned, other electrocardiographic abnormalities were seen which apparently resulted from previous infarction. Several of the subjects previously reported on with left bundle branch block evaluated at the School of Aviation Medicine illustrate this point.[6] At the time of clinical evaluation, each showed complete left bundle branch block. Four had previous normal electrocardiograms. In addition, two other subjects had previous abnormal electrocardiograms which were compatible with anterior myocardial infarction. The original tracings ruled out a congenital origin of the bundle branch

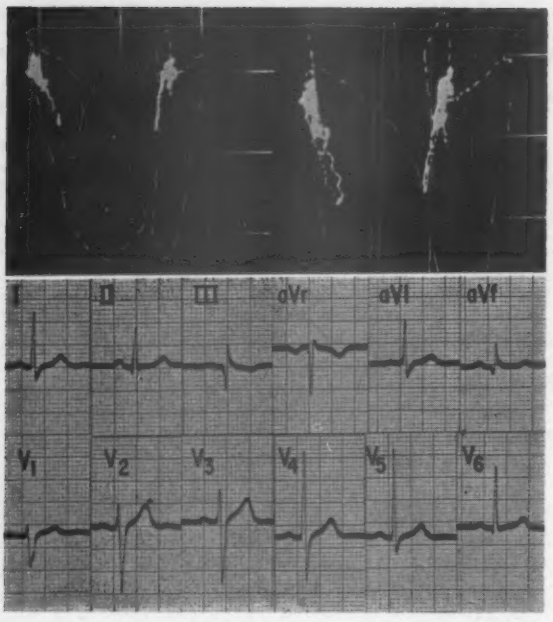


FIG. 1. Case 1. An electrocardiogram compatible with myocardial infarction of the inferior wall and a normal vectorcardiogram. There is a Q in leads II, III and aVF and the Q_3 is 0.04 second. The vectorcardiograms are (left to right) frontal plane, sagittal plane, center enlargement of frontal plane and center enlargement of the sagittal plane. The frontal plane is oriented as if one were facing the patient and the sagittal view is the same as a left profile view. An extracted Q_3 from the vectorcardiogram would have a duration of only 0.025 second which is insignificant.

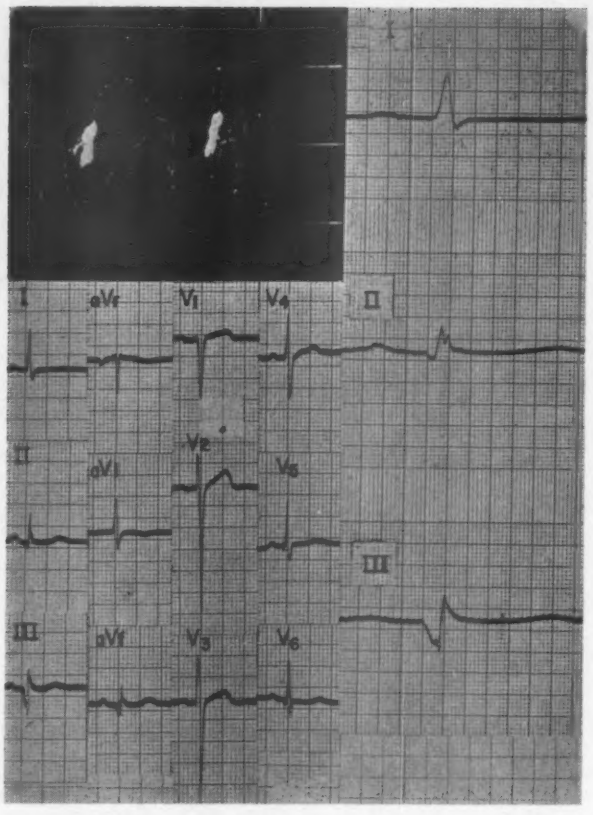


FIG. 2. Case 2. Frontal and sagittal views of the vectorcardiogram (*upper left*), electrocardiogram (*lower left*) and leads I, II and III recorded at 100 mm. per second (*right*). The routine electrocardiogram is abnormal with an isoelectric T_1 and a broad Q_3 of over 0.04 second in duration accompanied by a Q in leads II and aVF and upright P_3. The frontal plane of the vectorcardiogram shows the QRS loop directed away from a muscular area of the heart (electrically balanced lead III) for over 0.04 second, suggesting infarction of the inferior wall. In the vectorcardiogram the frontal plane is oriented as if one were facing the subject and the sagittal plane is a left profile view.

block in each case. There was no interim history which would suggest myocardial damage from an infectious disease or a metabolic disorder. For these reasons, each of these subjects is thought to have left bundle branch block secondary to a previous infarction.

Illustrative Cases

The following five illustrative cases serve to indicate some of the typical consultations at the School of Aviation Medicine.

CASE 1. *Normal Variation vs. Inferior Myocardial Infarction.* J. B. was a forty-two year old navigator. A routine electrocardiogram at the time of his annual physical examination was compatible with a myocardial infarction of the inferior wall (Fig. 1). He denied any symptoms referable to the cardiovascular system, and engaged in a reasonable amount of physical activity. There were no significant findings on physical examination. The electrocardiogram became relatively normal when recorded during inspiration, with marked diminution in the duration and amplitude of the Q waves in lead III. The vectorcardiogram with an electrically balanced lead system demonstrated that initial forces directed upward were of short duration and within normal limits. It was thought that these findings were insufficient to warrant the diagnosis of any disease.

Comment: Although this officer demonstrated an abnormal routine electrocardiogram which was compatible with infarction, thorough clinical investigation demonstrated no history or findings suggestive of infarction or impaired coronary circulation. The normal vectorcardiogram obtained with the electrically balanced bipolar reference system supports the concept that the electrocardiographic pattern resulted from factors of body build and electrical conductivity. This demonstrates that a single baseline abnormal electrocardiogram may not be sufficient basis for establishing the diagnosis of previous myocardial infarction.

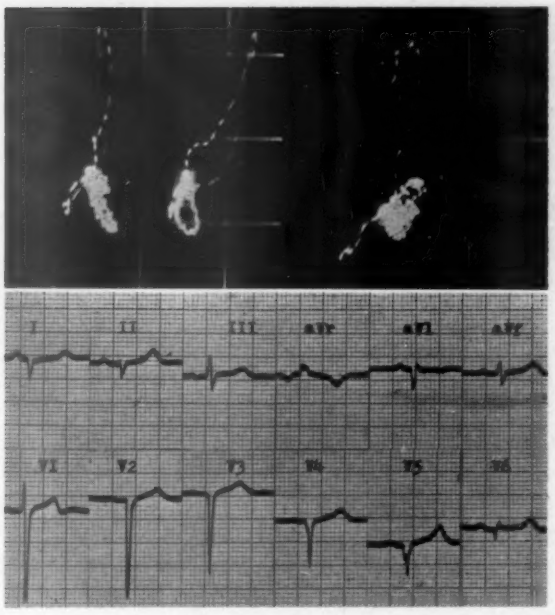


FIG. 3. Case 3. Frontal, sagittal and horizontal plane vectorcardiograms (*upper panel*). The latter vectorcardiogram is enlarged. The electrocardiogram (*lower panel*) and vectorcardiogram are abnormal, compatible with anterolateral myocardial infarction. The QRS loop in the transverse plane is inscribed in a clockwise fashion and directed posteriorly, just opposite to the normal vectorcardiogram.

CASE 2. *Silent Inferior Myocardial Infarction.* W. H. was a forty year old pilot who had a routine electrocardiogram at the time of his annual physical examination. This record demonstrated a deep Q wave of 0.04 second duration in lead III, with Q waves in leads II and aVF (Fig. 2). Thus, the record was compatible with infarction of the inferior wall, and it was requested that this officer be clinically evaluated. His past history was non-contributory for cardiovascular disease or for symptoms suggesting coronary occlusion. His physical activity was moderate. Electrocardiograms and quantitative vectorcardiograms demonstrated abnormal ventricular excitation and recovery, with the T forces directed away from the QRS forces. These findings were considered compatible with myocardial infarction of the inferior wall.

Comment: The clinical procedures for evaluating a person with an abnormal electrocardiogram did not provide information which would permit the exclusion of the diagnosis of healed myocardial infarction. The demonstration of an abnormal vectorcardiogram using an electrically balanced reference system plus the persistence of the abnormality with inspiration suggests that the abnormality cannot be attributed to body build, electrical conduction or position of the heart. This officer is one of a group of seventeen persons in whom the diagnosis of previous infarction has been established or could not be excluded.

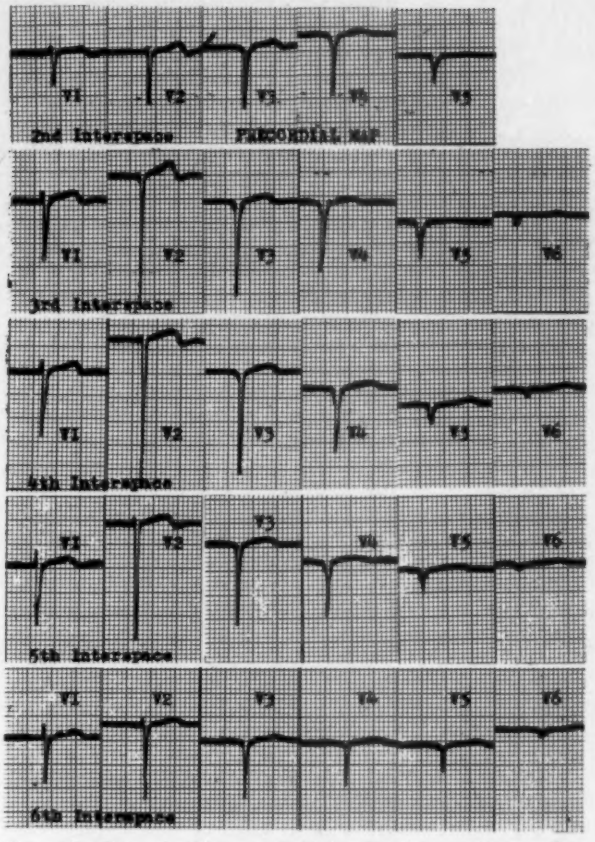


FIG. 4. Case 3. A precordial map demonstrates that the QS deflections in the precordial leads are not due to electrode position or are they confined to an isolated area.

CASE 3. *Silent Anterior Myocardial Infarction.* J. W. was twenty-three years old when a routine electrocardiogram was obtained for the repository. The record was grossly abnormal with a large deep Q wave over 0.04 second in duration in leads I, aVL and V_6 with QS deflections in leads V_3, V_4 and V_5 (Figs. 3 and 4). He was completely asymptomatic with no significant past history suggestive of infarction, myocarditis or trauma. Family history was non-contributory. Results of physical examination were negative with the exception of slight obesity with a height of 70 inches and weight of 192 pounds. The blood cholesterol was 267 mg. per cent.

Evaluation included a vectorcardiogram which was abnormal. The initial portion of the QRS loop moved rightward followed by a posterior course. This resulted in a transverse plane opposite to that seen in the normal vectorcardiogram. A precordial map (Fig. 4) demonstrated persistent QS deflections in leads V_3, V_4 and V_5 regardless of which interspace was used. A double Master exercise test was normal.

Comment: This grossly abnormal electrocardiogram could only result from damage to

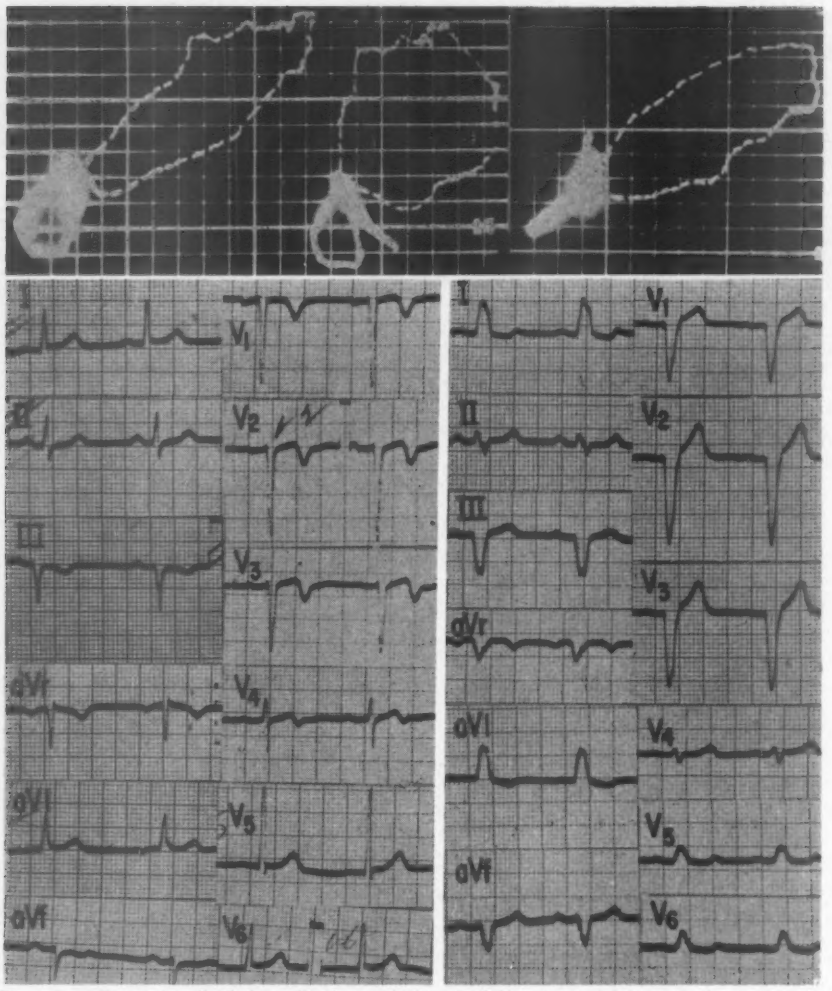


FIG. 5. Case 4. Left bundle branch block following abnormal electrocardiogram compatible with infarction of the anterior wall. Frontal, sagittal and horizontal plane vectorcardiograms showing left bundle branch block (*upper panel*). The QRS loop is directed posteriorly in the sagittal plane. In the transverse plane the initial component is directed posterior and to the left inscribing a clockwise loop. The electrocardiogram (*lower left*) was obtained routinely and is grossly abnormal. The subsequent tracing one year later taken at the same time as the vectorcardiogram (*lower right*) demonstrates left bundle branch block.

the anterolateral myocardial wall. The most likely cause is coronary artery disease. Congenital variation in the coronary arteries, trauma and rare diseases cannot be excluded. The value of the electrocardiogram in detecting such a case in a young asymptomatic subject is clearly pointed up here. This is one of the few cases in which we felt an anatomic diagnosis was permissible on the basis of the electrocardiogram or vectorcardiogram alone.

CASE 4. *Silent Anterior Infarction Followed by Left Bundle Branch Block.* L. D. was a thirty-one year old pilot who had a routine electrocardiogram recorded in 1957 at the time of his annual physical examination. This record demonstrated rudimentary R waves in leads V_1, V_2 and V_3 with inversion of the T waves in the same leads (Fig. 5). These findings were strongly suggestive of myocardial infarction of the anterior wall, and it was requested that he be evaluated clinically. He gave no history suggesting any cardiovascular disease, had no symptoms referable to the heart and appeared to be in good health. In March 1957, he fell from a truck and sustained a linear fracture of the occiput, with transient neurologic signs. Except for amnesia for a twenty-four–hour period following the accident, neurologic follow-up examination six months later was normal.

He was removed from flying status at the time of the injury to the head but was seen at the School of Aviation Medicine in November 1958 for evaluation of his cardiovascular status and the abnormal elec-

trocardiogram. Results of physical examination were negative except for a grade 1 (scale of 6) systolic murmur along the left sternal border and at the apex. The electrocardiogram revealed complete left bundle branch block.

Comment: The features of an asymptomatic myocardial infarction which occurred in a pilot thirty-one years of age, followed by the development of left bundle branch block, are present here. The infarction was entirely without symptoms, but was manifested by the initial electrocardiogram and the subsequent development of complete left bundle branch block. Without the previous abnormal electrocardiogram, one might have been misled into thinking that left bundle branch block in this young subject of healthy appearance was innocuous and without importance.

CASE 5. *Acute Myocardial Infarction.* S. B. was a twenty-four year old navigator in good health until July 1958. After vigorous exercise for about forty minutes, to which this officer apparently was accustomed, he drank a bit of cold water. About ten minutes later, he noted the onset of a dull ache in the mid-sternum with radiation to the left shoulder and arm. This pain changed in intensity, but one hour later was of sufficient severity to cause him to seek medical treatment. Blood pressure was noted to be 150/102 mm. Hg, pulse was 104 per minute, serum glutamic oxaloacetic transaminase (SGOT) was 150 units and the electrocardiogram showed elevation of the S-T segments in leads II and III. Pain gradually disappeared, the SGOT level returned to 20 units within three weeks and the electrocardiogram underwent serial changes with subsidence of the S-T segment changes and the T wave inversion.

This officer was seen at the School of Aviation Medicine two months after the acute episode, at which time he was entirely asymptomatic. Results of general physical examination were normal and laboratory procedures revealed no abnormalities. The electrocardiogram revealed a normal sinus rhythm with a rate of 60 per minute. All intervals were normal. The mean QRS axis was +75 degrees with transition at lead V_4. Mean T axis was −15 degrees with inversion of the T waves over the anterior precordium. There was a variable Q wave in leads II, III and aVF. This record was considered compatible with myocardial infarction of the inferior wall, and this was substantiated by the quantitative vectorcardiogram.

Comment: The residual changes in this officer's electrocardiogram two months after his acute episode were slight and could disappear completely with more time. It is interesting to speculate on the etiology of the infarction. A baseline electrocardiogram taken for the Electrocardiographic Repository in January 1958 was normal except that it demonstrated atrial rhythm with diphasic P waves in leads II, III and aVF. Serial records taken during his hospitalization showed similar intermittent variation in the location of the pacemaker.

The presence of an intermittent atrial rhythm suggests the presence of vagal inhibition in displacing the normal pacemaker. It might be assumed that such a cardiovascular response to vagal stimuli was rather marked. Coupled with this is the observation that this officer was accustomed to vigorous exercise, and that his pain was precipitated by drinking cold water, which may produce vagal stimulation. Two possible results might be expected from such strong vagal stimuli: sufficient bradycardia might occur to produce coronary insufficiency; or the major coronary vessels might be constricted to a degree which could produce acute coronary insufficiency. It is true that a large number of myocardial infarctions in young people are associated with coronary artery disease. On the other hand, the role of reflex (vagal) mechanisms in the production of coronary insufficiency with subsequent myocardial infarction in young subjects has not been adequately investigated, and frequently is not considered as a possible etiology.

COMMENTS

The military flying population is a highly selected one, and is required to meet rigid physical standards. These subjects have been carefully screened on initial selection and by periodic examination, so it may be assumed that those with symptoms, history or physical findings suggestive of myocardial infarction have been excluded. The military flying population is not comparable with any reported in the literature. The latter are either self-selected (as by symptoms in Yater's series[4]), or have different age distribution (as in Gould's[7] and Landman's[8] series).

It has not been common for the School of Aviation Medicine to evaluate flying personnel in whom the classic signs and symptoms of myocardial infarction develop. Those who survive are not suitable for flying duties and are relieved from such duty without reference to the School. Occasionally, inaccurate diagnoses or unrecognized histories have resulted in referral for evaluation. Lamb and Kable[9] have reported the case of a twenty-one year old aviation cadet who suffered an extensive antero-

lateral myocardial infarction. However, Air Force regulations now require that electrocardiograms of flying personnel be forwarded to the USAF Electrocardiographic Repository at the School of Aviation Medicine. To the extent that this procedure is followed by Air Force physicians, the Repository will develop a longitudinal study of the occurrence of myocardial infarction in the Air Force flying population that can be detected by serial electrocardiograms.

More commonly seen are subjects referred for evaluation of borderline electrocardiograms, but who give no history of cardiovascular disease, have had no symptoms referable to the cardiovascular system and who lead active lives in the military service.

Incidence and Symptoms of Coronary Sclerosis and Myocardial Infarction in Young Men: Experience with this type of patient at the School of Aviation Medicine confirms two important views which have now become well established in the medical literature, and which are enjoying increasing acceptance by physicians:

(1) *Arteriosclerosis of the coronary arteries of a degree which probably impairs coronary circulation occurs in a sizeable percentage of young men, and may cause myocardial infarction.*

In evaluating the incidence of myocardial infarction, the criteria for diagnosis must be carefully examined. Many of the previously reported series have excluded persons who did not have a "typical history" (Master, Dack and Jaffe[10] and Yater et al.[4]). For this reason these persons must of necessity be symptomatic. Thus, atypical cases and cases of silent infarction have frequently been excluded from incidence figures.

Glendy, Levine and White[2] reported a series of 100 patients less than forty years of age with coronary artery disease. Their age distribution was as follows:

Age (yr.)	Men	Women
20–29	7	1
30–34	17	0
35–39	72	3
Average	35.7	33.2

Master, Dack, and Jaffe[10] reported on 500 patients with coronary occlusion. Ten patients were less than thirty years of age at the time of their initial attack. It must be assumed that all these were symptomatic. French and Dock[3] reported eighty fatal cases of uncomplicated coronary lesions (all occurring in men). The age distribution of their cases was as follows:

Age (yr.)	No. of Cases
20–22	5
23–25	9
26–28	11
29–31	14
32–34	21
35–36	20

Yater et al.[4] reported the age distribution of 866 patients with myocardial infarction (450 fatal cases with autopsy confirmation, including the eighty cases previously reported by French and Dock[3]), as shown in Table III. Enos, Holmes and Beyer[11] reported the findings in 300 apparently healthy American soldiers killed in action in Korea. Although the ages of these soldiers ranged from eighteen to forty-eight years, with an average age of 22.1 years, the authors found gross evidence of coronary disease in 77.3 per cent, and found 70 per cent or greater occlusion of a coronary artery in 10.6 per cent.

(2) *Myocardial infarction of a size sufficient to produce definite changes in serial electrocardiograms may occur without symptoms or with such vague symptoms that they are not considered to be related to the heart.*

TABLE III

Age Distribution of 866 Cases of Myocardial Infarction, of the Total U. S. Army, and the Relative Incidence of Infarction, by Five-Year Age Groups*

Age (yr.)	Infarcts (%)	Total Army (%)	% of Cases per 1,000 Population	Relative Incidence
Less than 20	0.1	7.9	0.012	1
20–24	7.4	37.7	0.197	16:1
25–29	16.4	30.2	0.543	45:1
30–34	31.4	16.3	1.914	160:1
35–39	44.7	5.9	7.576	731:1

* Data from Yater et al.[4]

Herrick[1] described the clinical features of acute coronary occlusion in 1912. The pain associated with myocardial infarction has been described in great detail, and has become so intimately associated with the diagnosis that many of the series which deal with incidence of myocardial infarction will exclude all patients that do not have "typical symptoms." Gould[7] expressed a variation of this idea when he stated: "Nearly all the patients with fresh myocardial infarction who do not suffer cardiac pain give a history of dyspnea or weakness."

French and Dock[3] commented: "It should be emphasized, however, that only 6 of the 39 men whose hearts showed old areas of fibrosis had reported any complaint prior to the fatal attack; hence, it is possible that the actual incidence of coronary disease in the age group under analysis is much more frequent than is suggested by clinically recognizable and fatal cases." Thus, thirty-three patients in their series of eighty had experienced previous myocardial infarction without reported symptoms.

Landman et al.[8] studied asymptomatic myocardial infarction. In reviewing the clinical history of 255 patients who showed evidence of myocardial infarction at autopsy, they found that pain, shock, dyspnea and congestive failure had been absent during life in twenty-eight persons (11 per cent). All were persons over forty years of age. Zinn and Cosby[12] reported a series of 679 myocardial infarctions discovered during the performance of 5,076 autopsies. They commented: "It was recognized early in this series that 20 per cent of myocardial infarctions seen at the autopsy table were not clinically or electrocardiographically recognized."

Stokes and Dawber[13] reported that in the first four years of the study of 5,209 residents of Framingham, Massachusetts, there were sixty-seven persons between the ages of thirty and fifty years in whom definite electrocardiographic evidence of myocardial infarction developed. Six (9 per cent of the infarctions) had vague pains or other symptoms of varying degrees of severity which were not interpreted by the patient or the attending physician as manifestations of infarction. They concluded: "A significant proportion of myocardial infarctions are clinically unrecognized." In a later report of the same study, they noted that 20 per cent of the seventy-three myocardial infarctions occurring in the 5,209 subjects were clinically unrecognized.[14] In addition to the seventy-three cases of myocardial infarction, twenty persons died suddenly under circumstances that strongly suggested the presence of myocardial disease. The electrocardiogram returned entirely to normal in nine of the forty-nine patients (18 per cent) who survived a recognized infarction. It might be assumed then that four additional patients sustained infarction, but had neither characteristic symptoms nor the electrocardiographic residual.

Gould and Cawley[15] reported the incidence of infarction in 5,000 consecutive autopsies. They found myocardial infarction in 588 patients (11.8 per cent of all autopsies). They found "old, unsuspected" infarction in 175 (29.8 per cent of all infarctions). Electrocardiograms were available for fifty-six persons with "old, unsuspected" infarctions, and were "normal" in twenty-three cases, and "abnormal" but not diagnostic of infarction in the other thirty-three cases. The authors stated: " . . . (silent infarctions) represent 30 per cent of all infarcted hearts encountered at autopsy. This finding indicates that a myocardial infarction is often well tolerated by the patient. (Since the average age was seventy-one years) . . . it is evident that these patients may live out their expected life span."

Johnson et al.[16] reported 143 cases in which the presence of acute or healed myocardial infarction was established at necropsy. They noted that of 113 patients with healed infarctions, fifty-six (50 per cent) had no clinical diagnosis or recorded suspicion of previous myocardial infarction. Even among the group of patients who were seen repeatedly, 41 per cent had no history of angina pectoris or of previous acute substernal pain, even though severe coronary atherosclerosis and gross myocardial scars were present at necropsy.

Electrocardiographic Diagnosis of Silent Myocardial Infarction: It would appear from these series that at least 25 to 30 per cent of all infarctions are undiagnosed clinically. For every two or three myocardial infarctions detected, there is another which is unrecognized as such. There is undoubtedly considerable overlapping between the electrocardiograms of normal healthy people and those who have suffered infarction. For that reason, it is not possible to formulate criteria which will differentiate all persons who have had infarctions from all those who have not, on the basis of a single electrocardiogram. The reports of Surawicz et al.[17] and of Weisbart and Simonson[18] show the

difficulties in attempting to do so in the diagnosis of infarctions of the anterior and inferior walls.

The vectorcardiogram is one of the examining technics useful in establishing the diagnosis of silent myocardial infarction. By using a system of three leads which are electrically perpendicular to one another and equilibrated in amplitude, it is possible to demonstrate the true spatial direction of the heart's electrical forces throughout the cardiac cycle. We[19] have developed and reported a balanced bipolar lead system for vectorcardiography which allows the undistorted recording of the electrical forces of excitation and recovery. This technic demonstrates that many electrocardiograms of the Q_2, Q_3, Q_{aVF} pattern which meet the criteria for myocardial infarction of the inferior wall are in fact the result of lead distortion and not the result of any significant electrical forces away from an infarcted area of muscle.[20]

Stress testing, in the form of exercise, is of limited value in substantiating or excluding the diagnosis of myocardial infarction. A normal Master exercise test, for example, does not rule out the existence of a previous healed myocardial infarction, but only indicates the adequacy of the coronary circulation. Conversely, an abnormal exercise tolerance test reflects a detectable compromise of coronary circulation during exercise, but does not establish the diagnosis of previous myocardial infarction and has limited predictive value in forecasting future infarctions. Over 30 per cent of subjects with previous known infarctions have normal double Master exercise tests.[21]

It is generally agreed that the most certain method of establishing the diagnosis of myocardial infarction from the electrocardiogram is by finding significant serial changes in the QRS complex, S-T segment and T waves. This necessitates recording of a baseline record on each subject at an early age, and periodic records thereafter, even in the absence of symptoms. The USAF Electrocardiographic Repository now possesses electrocardiographic records on more than 67,000 persons. As additional records are collected for these same people, this study will assume even greater importance in the detection of silent myocardial infarction, and will be of value for these subjects as they enter the older age groups. In addition, clinical and electrocardiographic follow up will provide the medical profession with valuable data, which will lead to more accurate appraisal of the incidence of silent infarctions in apparently healthy men and the prognostic implications of some "borderline" electrocardiographic findings that may indicate predisposition to coronary artery disease.

Summary

Myocardial infarction as a result of coronary artery disease is a disorder which has particularly ominous implications for military fliers. The effects of an impaired coronary circulation and of decreased oxygenation of the blood are cumulative, and can be expected to compromise the personal health of the flier so affected and the safety of flight.

Electrocardiograms have been recorded on more than 67,000 fliers in the U. S. Air Force. Abnormal electrocardiograms in this series have led to the detailed clinical evaluation of fifty-one subjects to determine whether or not they had previously suffered an infarction. Of these fifty-one, thirty-four were found to be entirely normal, but the remaining seventeen demonstrated clinical findings that could not be considered normal and they are thought to have had a previous myocardial infarction.

Experience with this series of patients confirms two opinions which have been previously expressed in the literature: (1) that arteriosclerosis occurs in young people, often to a degree that impairs coronary circulation and may produce a myocardial infarction; and (2) that a significant portion (usually estimated at 25 to 30 per cent) of all infarctions occur without symptoms or with vague symptoms that are not related to the heart.

References

1. Herrick, J. B. Clinical features of sudden occlusion of the coronary arteries. *J.A.M.A.*, 59: 2015, 1912.
2. Glendy, R. E., Levine, S. A. and White, P. D. Coronary disease in youth. *J.A.M.A.*, 109: 1774, 1937.
3. French, A. J. and Dock, W. Fatal coronary arteriosclerosis in young soldiers. *J.A.M.A.*, 124: 1233, 1944.
4. Yater, W. M., Traum, A. H., Fitzgerald, R. P., Gresler, M. A. and Wilcox, B. B. Coronary artery disease in men eighteen to thirty-nine years of age. *Am. Heart J.*, 36: 334, 481, 683, 1948.
5. Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
6. Lamb, L. E., Kable, K. D. and Averill, K. H. Electrocardiographic findings in 67,375 asymptomatic subjects. V. Left bundle branch block. *Am. J. Cardiol.*, 6: 130, 1960.

7. Gould, S. E. and Cawley, L. P. Unsuspected healed myocardial infarction in patients dying in a general hospital. *Arch. Int. Med.*, 101: 524, 1958.
8. Landman, M. E., Anhalt, H. S. and Angrist, A. Asymptomatic myocardial infarction. *Arch. Int. Med.*, 83: 665, 1949.
9. Lamb, L. E. and Kable, K. D. Acute myocardial infarction in a twenty-one year old aviation cadet. *J. Aviation Med.*, 29: 263, 1958.
10. Master, A. M., Dack, S. and Jaffe, H. L. Age, sex, and hypertension in myocardial infarction due to coronary arteriosclerosis. *Arch. Int. Med.*, 64: 767, 1939.
11. Enos, W. F., Holmes, R. H. and Beyer, J. C. Coronary disease among United States soldiers killed in action in Korea. *J.A.M.A.*, 152: 1090, 1953.
12. Zinn, W. J. and Cosby, R. S. Myocardial infarction. I. Statistical analysis of 679 autopsy-proven cases. *Am. J. Med.*, 8: 169, 1950.
13. Stokes, J., III and Dawber, T. R. "Silent coronary": an analysis of the factors associated with clinically unrecognized myocardial infarction. *Circulation*, 16: 941, 1957. (Abstract.)
14. Stokes, J., III and Dawber, T. R. "Silent coronary": the frequency and clinical characteristics of unrecognized myocardial infarction in the Framingham study. *Ann. Int. Med.*, 50: 1359, 1959.
15. See reference 7.
16. Johnson, W. J., Achor, R. W. P., Burchell, H. B. and Edwards, J. E. Unrecognized myocardial infarction: a clinicopathologic study. *Arch. Int. Med.*, 103: 253, 1959.
17. Surawicz, B., Van Horne, R. G., Urbach, J. R. and Bellet, S. QS- and QR- patterns in leads V_3 and V_4 in the absence of myocardial infarction: electrocardiographic and vectorcardiographic study. *Circulation*, 12: 391, 1955.
18. Weisbart, M. H. and Simonson, E. The diagnostic accuracy of Q_3 and related electrocardiographic items for the detection of patients with posterior wall myocardial infarctions. *Am. Heart J.*, 50: 62, 1955.
19. Lamb, L. E. and Smith, G. B. An electrically balanced bipolar vectorcardiographic reference system: lead analysis and lead synthesis using the dR factor. *Am. J. M. Sc.*, 237: 759, 1959.
20. Smith, G. B., Jr. and Lamb, L. E. Vectorcardiography in aerospace flight. Applications and rationale. *Am. J. Cardiol.*, 6: 62, 1960.
21. Master, A. M., Friedman, R. and Dack, S. The electrocardiogram after exercise as a functional test of the heart. *Am. Heart J.*, 24: 777, 1942.

Electrocardiographic Findings in 67,375 Asymptomatic Subjects

X. Normal Values*

CAPT. ROLAND G. HISS, MC, USAF, LAWRENCE E. LAMB, M.D., F.A.C.C. *and* MARGARET F. ALLEN, M.S.

San Antonio, Texas

MANY studies have been conducted to describe the normal electrocardiogram and to delineate the range of variation of its several component parts. Each of these studies has added greatly to the understanding of electrocardiography and has enhanced the utility of the electrocardiogram as a diagnostic tool in clinical practice. The problem of what may be expected as normal variation and what must be viewed with suspicion, however, is far from settled.

Many previous analyses have outgrown their usefulness. Some investigations[1,2] were conducted before the precordial and augmented unipolar limb leads were introduced, and normal values so obtained have limited value in interpretation of the twelve-lead electrocardiogram in common use today. Others were based on a relatively small population and thus have statistical limitations in defining the numerous variables of the electrocardiogram. The Criteria Committee of the New York Heart Association[3] attempted to overcome this shortcoming by compiling the statistics of several authors into one set of tables. Electrocardiograms recorded by a number of technics and interpreted in a variety of ways on a heterogeneous group of subjects were combined. Useful application of pooled statistics of this type to the general population is difficult. Simonson[4] has elaborated on these criticisms.

Electrocardiograms obtained on 67,375 asymptomatic men in the U. S. Air Force have made available a large number of normal records.[5] The tracings in this highly select group of men provide a unique source from which data on the normal electrocardiogram can be obtained and also afford an opportunity to determine normal electrocardiographic variation at different age levels.

The purpose of this paper is to provide the frequency distribution, and other statistical data when applicable, to all parts of the electrocardiogram which are commonly assessed during diagnostic interpretation, and to separate these data into five-year age groups when there seemed to be variation with age.

MATERIAL AND METHODS

Approximately 1,000 records were chosen by a process of random selection for each five-year segment of the adult population from the mass of records on the U. S. Air Force flying personnel. The age groups are listed in Table I.

The necessity for including all subjects forty-five years of age and above in one group was due to the smaller number of subjects of this age in our total series. The first and last age groups do not represent a selection from the total survey, but rather all available normal records in these age ranges. The majority of the first age group (sixteen to nineteen years) consisted of aviation cadet applicants on whom a routine electrocardiogram was recorded as part of their selection physical examination. All other subjects in this study are subject to yearly physical examinations, stringent medical standards and close medical scrutiny by their respective flight surgeons. Thus, the incidence of significant cardiac disease would be expected to be as low or lower than most segments of the American population.

Selection of Records: Following basic selection by a random sampling method, electrocardiograms were excluded from the study if they showed any of the following diagnostic entities: sinus arrest with or

* From the Department of Internal Medicine, School of Aviation Medicine, The Aerospace Medical Center, Brooks Air Force Base, San Antonio, Texas.

TABLE I
Number of Records Analyzed in Each Age Group

Group No.	Age Range (yr.)	No. of Records Analyzed
1	16–19	1,077
2	20–24	931
3	25–29	926
4	30–34	825
5	35–39	903
6	40–44	805
7	Over 45	547
Total	16–58	6,014

without escape, any arrhythmia involving a pacemaker other than the sinoatrial node (which included all premature beats whether of supraventricular or ventricular origin), any A-V conduction defect (the upper limit of P-R interval was arbitrarily set at 0.20 second at the beginning of the study), significant intraventricular conduction defects such as the Wolff-Parkinson-White (WPW) syndrome, right bundle branch block and left bundle branch block, non-specific T wave changes and tracings with undeniable evidence of previous myocardial infarction. Records were not excluded if they demonstrated any one of the several minor electrocardiographic variations such as sinus tachycardia, sinus bradycardia, sinus arrhythmia, minor variations of intraventricular conduction, marked right or left axis deviation, marked increase or decrease in QRS voltage, variations in P wave contour or doubtful evidence of myocardial infarction. No record was excluded because of evidence suggestive of left ventricular hypertrophy, as it was our opinion that such a diagnosis on the basis of the electrocardiogram alone is always tenuous, and to exclude such tracings from a series of normal values might introduce a bias. Only one tracing was excluded because of electrocardiographic evidence of right ventricular hypertrophy; this tracing showed such extreme changes that a diagnosis of mitral stenosis was suspected. The diagnosis was later clinically confirmed.

Other tracings were excluded because technical error in the recording was so extreme that accurate reading of the various complexes could not be carried out. Tracings without all twelve routine leads were similarly excluded. The number of tracings in each of the seven age groups which were finally selected for detailed analysis is given in Table I.

Most electrocardiograms in this study were recorded on a direct writing instrument. Since the records were made at numerous Air Force Bases throughout the world by a variety of technicians, they are comparable to records obtained in clinical practice. Although it might be argued that photographic instruments are more precise, it is a fact that they are not used as frequently as direct writing instruments. Thus, standards based on tracings obtained from direct writing instruments are more applicable to the common clinical situation.

Analysis of the record included determination of heart rate, P wave duration, P wave amplitude, P axis in the frontal plane, P-R interval, QRS duration, Q-T interval, Q-U interval, duration of the S wave in lead V_2, duration of the R wave in lead V_2, QRS axis in the frontal plane and transition in the precordial leads, axis of the S-T segment vector and its greatest amplitude in the frontal plane, determination of the S-T segment elevation in the precordial leads and its greatest amplitude, T axis in the frontal plane and transition in the precordial leads, QRS amplitude in leads I, aVF, V_2 and V_6, T wave amplitude in the same four leads, the spatial QRS-T angle, the presence or absence of Q waves in leads I, II, III, aVL and aVF, their duration and amplitude when present, the presence or absence of the S_1S_2 and the $S_1S_2S_3$ configurations, and a tabulation of the ratio of R to S waves in leads V_1 and V_2 when greater than 1. All measurements of amplitude were corrected for standardization (1 cm. = 1 mv.). The height and weight of each of the subjects whose electrocardiograms were studied were nearly always obtained. The age was known in all cases. These data were entered on IBM cards for statistical tabulation. Several mathematical calculations relative to QRS and T wave amplitude were later performed.

The detailed reading was performed by one of us and five electrocardiographic technicians trained for the project. A uniform method for each determination was agreed upon and the first 1,000 tracings were read by a technician and one of us so that variations of technic between the readers were resolved at the onset.

Finally, the results were tabulated as percentage distributions for each age group. Determinations of the first, second and third quartile* were made in all instances, but are presented only for those determinations which differed from one age group to the next. A large number of bivariate distributions were compiled whereby the frequency of one variable with respect to another was compared. Much of the data relative to QRS amplitude, QRS axis, age and body weight were subjected to statistical analysis with determination of correlation coefficients. The frequency distributions and quartiles are presented in tabular form. The statistical correlations appear in the body of the text.

* The three quartiles separate an ordered series into four equal parts so chosen that 25 per cent of the series had a value no greater than the first quartile, 50 per cent had a value no greater than the second quartile and 75 per cent had a value no greater than the third quartile. The second quartile is the median.

TABLE II
Height in Inches
Quartiles by Age Group

Quartile	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
First	68 1/2	68 3/4	68 3/4	68 1/2	68 1/2	68	68 1/4	68 1/2
Second	70	70 1/4	70 1/2	70	70	70	70	70 1/4
Third	71 3/4	72	72 1/2	72	71 1/2	71 3/4	71 1/2	72

TABLE III
Body Weight in Pounds
Quartiles by Age Group

Quartile	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
First	143	150	155	157	159	160	160	153
Second	154	162	168	172	172	174	173	168
Third	169	178	181	184	185	187	187	182

TABLE IV
Relative Weight*
Percentage Distribution by Age Group

Relative Weight Categories	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
1	10.9	4.5	1.7	1.3	0.3	0.4	0.8	3.3
2	19.7	11.6	8.9	5.1	4.6	3.1	2.3	8.7
3	43.0	41.5	37.8	32.5	28.5	26.4	27.7	34.8
4	15.4	20.4	21.6	22.3	26.1	24.0	24.6	21.6
5	11.0	22.0	30.1	38.8	40.5	46.2	44.7	31.6
Number of persons weight unknown	20	23	23	28	25	21	30	170

* For explanation of relative weight definition, see text.

RESULTS

Height: The range of height of the subjects in this study was 62 to 77 inches. There was no apparent variation with age. Table II shows the first, second and third quartiles for height by age group.

Weight: The upper and lower extremes of body weight were 100 and 269 pounds. The quartiles by age group are given in Table III. Figure 1 shows the percentage distributions of weight by age group. It is of interest to note the increased number of heavier subjects in the older age groups. Further comment on this finding will be given in the section on QRS amplitude.

Relative Weight: All subjects were divided into one of five relative weight categories based on standard height-weight tables given in Air Force Manual 160-1.[6] The standards for the twenty-six- to thirty-year bracket were used for all subjects regardless of their age. We were of the opinion that a sliding scale of allowable

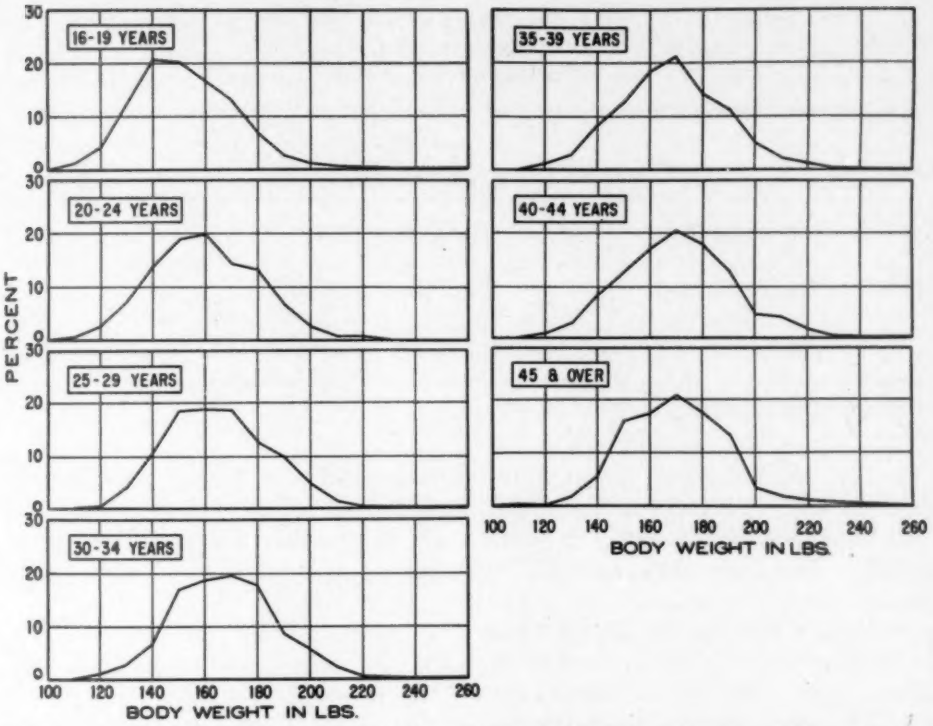


FIG. 1. Percentage distribution of body weight within each age group. Each point on the plot includes the per cent of subjects with weights up to 9 pounds above the corresponding abscissa value. For instance, a point corresponding to 140 pounds includes all subjects weighing up to 149 pounds. Note the increase in percentage of heavier subjects with each older age group.

increased weight with increased age would unjustifiably mask a great deal of obesity found in the older persons. The five categories were defined as follows: category 1, standard weight for a given height minus 20 pounds or more; category 2, standard weight for a given height minus 10 to 19 pounds; category 3, standard weight for a given height plus or minus 9 pounds; category 4, standard weight for a given height plus 10 to 19 pounds; and category 5, standard weight for a given height plus 20 pounds or more.

Table IV gives the percentage distribution of these five categories within each age group and Figure 2 shows the percentage of normal (category 3), underweight (categories 1 and 2) and overweight (categories 4 and 5) subjects. There was a marked increase of relative weight with increased age. A comparison of relative weight to height and heart rate revealed no marked relation.

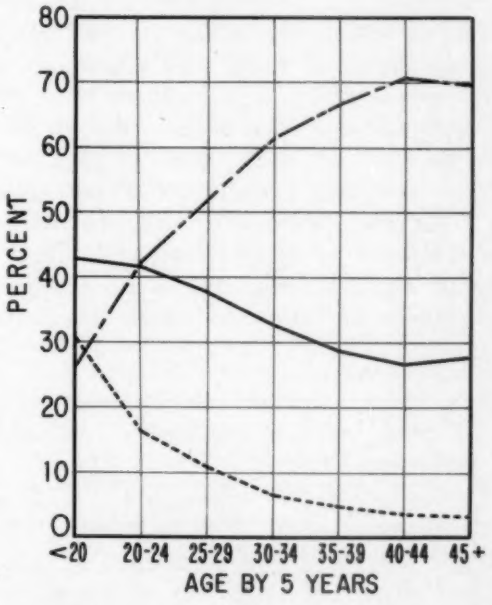


FIG. 2. Percentage distribution of relative weight within each age group. Solid line represents subjects plus or minus 9 pounds of their standard weight for a given height. Broken line represents subjects 10 pounds or more underweight for their height. Dash-dot line represents subjects 10 pounds or more overweight for their height. Standards are based on the twenty-six to thirty-year group of the height-weight table given in AFR 160-1.[6]

HEART RATE

The heart rate was determined in leads II and V_2, with the latter used as the arbitrary heart rate for the entire tracing. The heart rate for the standard bipolar extremity leads

TABLE V
Heart Rate*
Quartiles by Age Group

Quartile	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
First	58	59	60	60	63	63	62	61
Second	66	66	67	68	70	70	70	68
Third	76	74	75	76	77	78	78	77

* Heart rate measured in beats per minute in lead V_2.

(which are usually recorded first) often is increased when compared to the precordial leads. This is a result of anxiety which tends to abate during recording. The heart rate in lead V_2 is a more reliable index of the usual rate. The range of heart rates was from 39 to 129 beats per minute. Table v gives the quartiles by age group of heart rate and Figure 3 shows the per cent of subjects in each age group with heart rates of less than 60 per minute. There was only a slight decrease in the per cent with a heart rate of less than 60 per minute from the youngest to the oldest age group. The decrease in bradycardia with advancing age was not as marked as found by Packard et al.[7] in their follow-up study of 1,000 Naval aviators originally investigated by Graybiel et al.[2] When these subjects were first studied they were between twenty and thirty years of age, and 39 per cent had heart rates below 60 per minute; only 6 per cent of the same subjects had heart rates this low ten years later. The slight increase of heart rate with age in our series compares favorably with the data obtained by Simonson and Keys,[8] who noticed a decrease of only 0.016 second of the mean R-R interval in their older subjects (forty-five to fifty-five years) as compared to their younger subjects (eighteen to twenty-five years).

Heart rates in each age group were compared to the corresponding heights and weights in the form of bivariate frequency distributions. There was no apparent relation of either height or weight to heart rate and these data are therefore not presented.

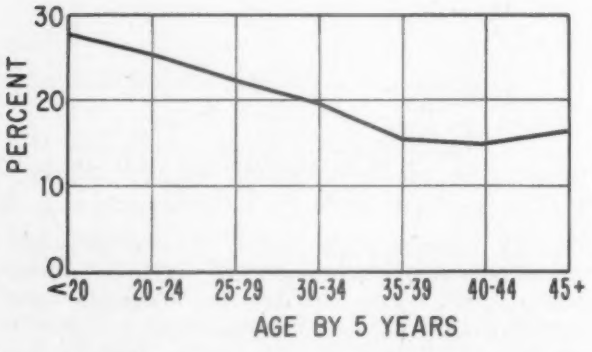


FIG. 3. Percentage of subjects with heart rates less than 60 beats per minute in each age group. This slight decrease in the incidence of bradycardia reflects decrease in vagal tone with age.

P WAVE

Duration: The duration of the P wave was measured from that point at which the baseline was first interrupted by an upward deflection until it returned. The longest P wave duration in any limb lead was determined; it was usually in lead II. Table VI gives the percentage distribution of P wave duration for the entire series; there was no apparent variation with age.

The range of P wave duration varied from 0.06 through 0.15 second; the median was 0.11 second with the first and third quartiles

TABLE VI
Greatest P Wave Duration in Frontal Plane
Percentage Distribution of Entire Series*

Greatest P Wave Duration in Frontal Plane (sec.)	Per Cent
0.06–0.07	0.3
0.08–0.09	17.6
0.10–0.11	54.4
0.12–0.13	26.4
0.14–0.15	1.3

* There was no apparent variation among age groups.

TABLE VII
Greatest P Wave Amplitude in Frontal Plane
Percentage Distribution of Entire Series*

Greatest P Wave Amplitude in Frontal Plane (mv.)	Per Cent
0.05	31.2
0.10	49.9
0.15	15.8
0.20	2.9
0.25–0.35	0.3

* There was no apparent variation among age groups.

TABLE VIII
P Axis in Frontal Plane
Percentage Distribution of Entire Series*

P Axis in Frontal Plane (degrees)	Per Cent
−30	0.3
−15	0.3
0	3.8
+15	5.4
+30	12.3
+45	31.6
+60	25.3
+75	20.9
+90	0.1

* There was no apparent variation among age groups.

0.10 and 0.12 second, respectively. The mode was 0.10 second. These values are somewhat higher than listed by other authors.[1,2,9] The method of determination of this value is partly responsible for discrepancies between various series. Also, some previous studies were performed on photographic records of three limb leads. In this series these values were obtained from direct writing instruments using all six limb leads.

Amplitude: P wave amplitude and all other amplitudes were measured using the bottom edge of the stylus line as the reference point. In this way, the thickness of the line did not influence the amplitude measurements. The greatest P wave amplitude of any extremity lead was utilized, which in most cases was lead II. Selecting the greatest P wave amplitude regardless of the limb lead in which it appeared avoided the problem of misleading statistics resulting from discrepancy between a lead axis and the axis of the vector concerned. Simonson[4] has pointed out the potential error in determining normal ranges for values on an individual lead basis; for example, the P wave amplitude in lead I might be small if the P axis were +75 degrees, but would be large if the P axis were +15 degrees. Determination of meaningful normal values for P wave amplitude in lead I would have to consider the P axis and the resulting table would be cumbersome. Since the object of assessing P wave amplitude is to evaluate the greatest measurable voltage created by atrial activation, the greatest P wave amplitude seen in any lead is critical.

The values recorded in Table VII do not show age breakdown as there was no apparent variation between age groups. The range of P wave amplitude was 0.05 through 0.35 mv. with most records falling between 0.05 and 0.15 mv. These values are in general agreement with those given by Stewart and Manning,[1] but are higher than those listed by the Criteria Committee of the New York Heart Association.[3] However, all previous series have been conducted on an individual lead basis, and our data may be compared only in an approximate way.

P Axis in the Frontal Plane: The axis of the P vector in the frontal plane was determined by using the standard hexaxial reference system. The percentage distribution for different P axes in the entire series is presented in Table VIII. There was no visible variation between the several age groups. The range was −30 through +90 degrees with 95 per cent of the subject population falling between the range of +15 through +75 degrees. The mode was +45 degrees and the median the same. Comparison of the P and QRS axes in the same record revealed a general trend, that is, vertical P axes were associated with vertical QRS axes, and horizontal P axes with horizontal QRS axes.

Inclusion of records in this series with P axes of −15 and −30 degrees might be questioned on the grounds that these records are actually not normal, but represent atrial rhythm or a lower focus within the S-A node. This cannot be disputed, but arrhythmias of this kind are so insignificant that their inclusion within the normal range is probably justified. Comparable data on P axis from previous studies on normal values are lacking.

P-R INTERVAL

The P-R interval was measured according to the method suggested by the Criteria Committee of the

TABLE IX
P-R Interval
Percentage Distribution by Age Group

P-R Interval (sec.)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
0.10–0.11	0.3	0.4	0.5	0.4	0.4	0.2	0.2	0.4
0.12–0.13	8.2	6.0	5.4	5.9	8.6	8.0	8.4	7.2
0.14–0.15	33.1	27.9	25.2	27.9	26.0	24.7	22.3	27.2
0.16–0.17	39.7	42.2	39.5	39.6	40.8	39.1	40.6	40.2
0.18–0.19	15.1	18.8	21.2	18.9	17.7	20.7	20.1	18.7
0.20	3.6	4.6	8.2	7.3	6.3	7.2	8.4	6.3

New York Heart Association,[3] namely, the longest interval in any of the six bipolar or unipolar extremity leads measured from the beginning of the P wave to the beginning of the QRS complex whether represented by a Q wave or an R wave. It is true that on certain occasions a P-R interval measured in this manner will be falsely prolonged when early forces of ventricular activation are perpendicular to a given lead. However, the error incurred here is very slight and, as the "criteria" states, the cumbersome procedure necessary to obtain a more exact value[10] is not worth the increased accuracy. Kossmann[11] pointed out that the longest P-R interval will be the same as that obtained by more exacting calculation in 97.4 per cent of cases.

Table IX shows the percentage distribution by age group for the P-R interval. The range for this value was 0.10 through 0.20 second. We considered P-R intervals above 0.20 second as representing first degree A-V block and excluded them from this analysis. The incidence of P-R intervals above 0.20 second in our population of 67,375 subjects is discussed in another article in this series.[12] The frequency of P-R intervals of 0.21 and 0.22 second was approximately two per 1,000 records and was less for longer P-R values. This points up the relative rarity of P-R intervals above 0.20 second and the validity of considering 0.20 second as the upper limit of normal for practical purposes. Several previous studies[1,2,9] have set the upper limit between 0.20 and 0.24 second.

There appears to be a slight increase in the frequency of longer P-R intervals in the older age groups. Comparison of P-R interval to body weight (regardless of age) indicated a slight trend toward longer P-R intervals in heavier subjects. The relation of P-R interval to height was random. The comparison of P-R interval to heart rate indicated a trend toward inverse relation, that is, longer P-R intervals associated with slower heart rates, but this relation was not strong.

P-R Interval Minus P Wave Duration: To determine standards for the relative value of the isoelectric segment between the end of the P wave and the beginning of the QRS complex, the P wave duration was subtracted from the concurrent P-R interval (Table X). There was no apparent variation between age groups. Approximately 10 per cent of all subjects in this series had a short isoelectric segment (0.03 second or less) between completion of atrial excitation and the onset of ventricular activation. This points up the fact that short P-R intervals are commonly seen in the absence of arrhythmias and the WPW syndrome.

Q-T INTERVAL

The Q-T interval was measured from the beginning of the QRS complex to the end of the T wave in the lead in which it was the longest.

TABLE X
P-R – P Interval
Percentage Distribution of Entire Series*

P-R – P Interval (sec.)	Per Cent
0.00–0.01	1.3
0.02–0.03	8.4
0.04–0.05	37.1
0.06–0.07	36.6
0.08–0.09	14.4
0.10–0.11	2.0
0.12–0.13	0.2

* There was no apparent variation among age groups.

TABLE XI
Q-T Interval
Percentage Distribution by Age Group

Q-T Interval (sec.)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
0.24–0.27	0.1	0.1	...	0.2	...	...	...	0.1
0.28–0.31	2.5	1.6	1.7	1.1	2.2	2.7	1.1	1.9
0.32–0.35	24.0	19.5	17.7	14.8	19.9	18.1	17.9	19.1
0.36–0.39	52.0	47.8	54.4	50.4	53.5	53.8	53.9	52.1
0.40–0.43	18.8	27.1	24.8	30.7	23.0	23.7	25.2	24.5
0.44–0.47	2.5	3.4	1.3	2.8	1.1	1.4	1.8	2.1

This was commonly lead V_2. Table XI gives the percentage distribution by age group for this interval; there does not appear to be a very remarkable variation between age groups. Simonson and Keys[8] noted a difference of only 0.01 second in the mean Q-T values between young and older subjects.

The range of the Q-T interval was 0.24 through 0.47 second; the median was 0.38 second for the entire series, and the mode was 0.36 through 0.39 second. This range is wider than those given by Stewart and Manning,[1] Graybiel et al.[2] and White et al.[13] As pointed out by Simonson,[4] the extremes of a range for normal will increase directly in proportion to the number of subjects included in the study. This accounts for the increase of range in our statistics to include Q-T intervals as short as 0.24 second.

The inverse relation of the Q-T interval to heart rate has been adequately described[11] and was again noted in this study. The variation of rate between age groups was so slight that calculation of a corrected Q-T interval (QT_c) was not carried out.

Q-U INTERVAL

The Q-U interval was measured from the beginning of the QRS complex to the end of the U wave in the lead in which this value was the greatest. In most instances this was lead V_2 or V_3. The Q-U interval determination is not accurate since many records have obscure U waves which cannot be separated from variations of the baseline. This limitation is recognized and the statistics given for the percentage distribution of Q-U interval in Table XII should be regarded only as approximate for this reason.

The range for the Q-U interval was 0.40 through 0.71 second, with the mode 0.56 through 0.59 second. The median was 0.56 second; the first and third quartiles 0.54 and 0.60 second, respectively. These values are in general agreement with those of Lepeschkin

TABLE XII
Q-U Interval
Percentage Distribution by Age Groups

Q-U Interval (sec.)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
0.40–0.43	0.5	1.0	0.2	0.6	0.8	1.1	0.2	0.6
0.44–0.47	3.7	1.6	1.5	1.0	2.2	1.6	0.9	1.9
0.48–0.51	13.6	6.4	5.7	6.9	5.2	6.2	5.7	7.4
0.52–0.55	29.3	29.0	23.8	18.8	24.7	21.2	20.5	24.4
0.56–0.59	36.3	37.8	42.9	37.6	44.2	42.0	40.2	40.0
0.60–0.63	13.2	17.8	20.8	29.8	20.6	23.6	28.7	21.3
0.64–0.67	3.1	4.9	4.9	5.0	2.3	3.6	3.8	3.9
0.68–0.71	0.3	1.4	0.2	0.4	...	0.6	...	0.4

TABLE XIII
QRS Duration
Percentage Distribution by Age Groups

QRS Duration (sec.)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
0.05	0.1	0.3	0.2	0.1	0.4	0.5	0.7	0.3
0.06	4.4	4.2	4.1	6.1	4.5	4.8	8.6	5.0
0.07	17.9	16.3	17.1	19.4	21.8	24.8	25.4	19.9
0.08	48.1	46.2	48.9	48.6	48.7	48.3	42.4	47.6
0.09	20.9	22.3	19.5	20.2	19.5	16.0	17.2	19.6
0.10	8.0	9.1	9.3	5.1	4.2	4.7	4.9	6.7
0.11	0.6	1.5	0.9	0.5	0.8	0.7	0.7	0.8

and Surawicz[14] who found the range of Q-U intervals in 100 normal subjects was 0.44 through 0.68 second. There appears to be some increase of the Q-U interval in our series with age. For instance, 47.1 per cent of the first age group had a Q-U interval of 0.55 second or less, whereas only 27.3 per cent of the last age group had a Q-U interval of this amount or less.

QRS COMPLEX

Duration: The QRS duration was determined in the lead which demonstrated the longest value. This was in most instances lead V_2 or V_3. Percentage distribution for this duration is given in Table XIII. The range was 0.05 through 0.11 second, and the mode was 0.08 second. There appeared to be some increase in the number of subjects with relatively prolonged QRS durations in the youngest age groups as compared to the older age groups. The percentage of the subjects under thirty years with a duration of 0.10 or 0.11 second was about twice as large as the percentage of the subjects over thirty years with these durations.

These values are in agreement with most studies, particularly those of Stewart and Manning[1] and Graybiel et al.[2] Kossmann's[11] statement that QRS duration above 0.10 second may be normal in some persons, but is often more indicative of heart disease, is corroborated by our figures. Only fifty subjects of the 6,014 analyzed had QRS durations longer than 0.10 second, such that they represent the extreme of normal variation. Although it is doubtful that any of these fifty subjects had significant heart disease, the relative rarity of this finding places a high index of suspicion on any patient who may show it. Graybiel et al.[2] reviewed the findings of eleven investigations of QRS duration performed prior to 1944. Most of these series included a few subjects with QRS durations of 0.11 or 0.12 second without evidence of heart disease. Lepeschkin and Surawicz[14] noted a direct relation between QRS duration and body height. Comparison of the QRS duration to height in our series corroborated the observations of these workers. Body weight and QRS duration did not appear to be related.

R Wave Duration in Lead V_2: The R wave duration in lead V_2 was determined in all tracings, and the over-all percentage distribution for this value is given in Table XIV. There appeared to be no apparent variation with age. The range was zero through 0.06 second with all quartiles at 0.03 second. Our purpose in obtaining these statistics was an attempt to delineate normal variation of intraventricular

TABLE XIV
Duration of R and S Waves in Lead V_2
Percentage Distribution of Entire Series*

Duration of Wave (sec.)	R Wave Duration in Lead V_2	S Wave Duration in Lead V_2
0.0	0.2	...
0.1	1.2	0.1
0.2	20.7	1.2
0.3	52.9	6.7
0.4	21.7	22.6
0.5	2.9	38.5
0.6	0.4	23.8
0.7	...	6.3
0.8	...	0.8

* There was no apparent variation among age groups.

TABLE XV
QRS Axis in Frontal Plane
Percentage Distribution by Age Group

QRS Axis in Frontal Plane (degrees)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
−90	...	...	0.1	...	...	...	...	0.02
−75	...	...	...	...	0.2	...	0.4	0.08
−60	...	0.1	...	0.4	0.2	0.1	0.9	0.2
−45	0.5	0.5	0.4	0.2	0.2	1.1	1.1	0.5
−30	0.3	1.6	0.5	1.0	1.2	1.4	2.4	1.1
−15	0.3	0.4	0.4	1.7	2.1	5.2	5.9	2.0
0	0.7	2.0	3.2	5.2	4.3	5.7	8.6	3.9
+15	1.1	2.9	3.8	4.0	9.6	9.4	10.6	5.5
+30	5.4	6.2	8.3	10.7	9.7	11.4	14.4	9.0
+45	7.6	12.4	12.5	20.9	21.6	22.0	17.6	15.8
+60	19.5	18.6	20.7	22.4	19.4	16.5	14.6	19.1
+75	40.1	38.3	36.2	24.4	24.8	20.7	18.6	30.2
+90	19.9	13.0	10.8	7.5	4.5	4.5	3.5	9.9
+105	3.8	2.4	1.9	1.5	1.1	1.2	0.9	2.0
+120	0.1	...	0.2	...	...	...	...	0.06
Indeterminate	0.7	1.5	0.8	0.2	0.9	0.6	0.5	0.8

conduction. Lead V_2 is an anteroposterior coordinate, or Z axis. An R wave in this lead represents electrical forces directed anteriorly and often means persistent electrical activity in the right ventricle.

S Wave Duration in Lead V_2: The frequency distribution for the duration of the S wave in lead V_2 for the entire series is also given in Table XIV. The range for the S wave in lead V_2 was 0.01 through 0.08 second with median and mode at 0.05 second. Variation with age was extremely slight, and amounted to a minimally increased frequency of prolonged S waves in the younger age groups as compared to the older age groups. This finding may be related to an increased incidence of physiologic hypertrophy in the younger subject.

QRS Axis in the Frontal Plane: The QRS axis in the frontal plane was determined on the basic hexaxial reference system. Determinations were made to the nearest 15 degrees as it is our opinion that this is the limit of accuracy obtainable from standard, unbalanced electrocardiographic leads. Table XV shows the percentage distribution for QRS axis in the frontal plane by age group, and Figure 4 provides a graph of the values. Table XVI provides the quartiles for each age group. (The quartiles were based on an arrangement of the values starting with the most negative, −90 degrees, and progressing clockwise to the most positive, +120 degrees, on the hexaxial reference system.)

There is a marked leftward shift of the QRS

TABLE XVI
QRS Axis in Frontal Plane
Quartiles by Age Group*

Quartile	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
First	60	45	45	45	30	30	15	45
Second	75	75	60	60	60	45	45	60
Third	75	75	75	75	75	75	60	75

* All figures shown are in degrees.

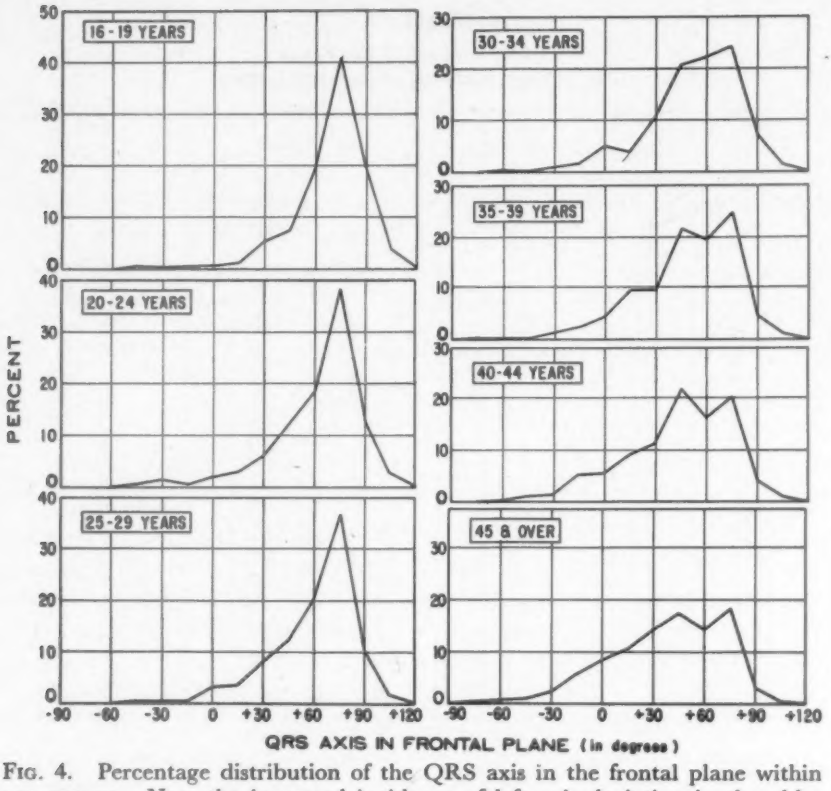


FIG. 4. Percentage distribution of the QRS axis in the frontal plane within age groups. Note the increased incidence of left axis deviation in the older age groups.

axis in the frontal plane with increasing age. This is first apparent between the first and second age groups. The first quartile for the first age group was +60 degrees, whereas the first quartile for the second age group was +45 degrees. Approximately 16 per cent of the first age group had QRS axes of +45 degrees or less, whereas approximately 26 per cent of the second age group are within this range. The range for QRS axis was −90 through +120 degrees with few subjects at the extremes. Our values are in general agreement with Stewart and Manning[1] and other series whose subjects are not differentiated by age. They are more closely comparable to the statistics of Graybiel et al.[2] and Packard et al.[7] The QRS axis mean in the first study was +61.6 degrees with a range of −35 through +120 degrees, whereas the QRS axis mean on the same subjects ten years later was +48.2 degrees with a range of −45 through +95 degrees. Their studies showed that increase in body weight and leftward rotation of the QRS vector were often associated, and that

TABLE XVII
QRS Transition
Percentage Distribution by Age Group

QRS Transition at Lead	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
V_1	1.3	4.8	7.5	7.9	8.6	7.8	8.8	6.4
V_2	22.4	24.2	25.8	23.5	27.1	29.7	27.8	25.5
V_3	58.0	50.3	48.6	49.7	49.1	47.2	49.9	50.7
V_4	15.6	17.8	14.9	17.0	13.6	13.2	12.4	15.1
V_5	2.4	2.4	2.7	1.7	1.6	1.5	1.1	2.0
V_6	0.1	0.4	0.1	0.1	...	0.6	...	0.2

TABLE XVIII
Q Wave Duration in Leads I, II, III, aVL and aVF
Percentage Distribution by Age Group

Lead	Q Wave Duration (sec.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I	None	85.1	76.5	74.3	68.4	68.1	56.8	67.8	71.9
	0.01	12.3	20.8	21.9	27.9	28.6	39.4	29.1	24.8
	0.02	2.5	2.7	3.7	3.8	3.3	3.9	3.1	3.3
	0.03	0.1	...	0.1	...	...	...	...	
II	None	51.6	51.5	46.3	48.6	54.2	51.1	67.1	52.1
	0.01	35.8	37.1	41.7	40.5	37.1	41.4	28.9	37.9
	0.02	11.2	11.4	11.4	10.4	8.4	7.5	4.0	9.6
	0.03	1.3	0.1	0.5	0.5	0.3	0.1	...	0.5
III	None	52.5	51.1	47.1	55.0	58.8	60.4	70.0	55.4
	0.01	25.8	29.1	32.4	27.6	24.0	25.3	18.5	26.6
	0.02	18.6	15.5	16.7	13.8	12.6	11.6	9.3	14.5
	0.03	2.9	4.2	3.7	3.4	4.3	2.6	2.0	3.4
	0.04	0.3	0.1	0.1	0.1	0.2	0.1	0.2	0.2
aVL	None	90.4	83.2	83.6	77.5	78.0	65.7	73.1	79.7
	0.01	6.3	12.9	11.7	18.3	18.4	29.2	23.2	16.2
	0.02	2.9	3.3	4.4	3.9	3.2	5.0	3.5	3.7
	0.03	0.4	0.5	0.3	0.4	0.4	0.1	0.2	0.3
aVF	None	51.9	50.8	48.9	52.2	56.9	55.7	68.6	54.1
	0.01	32.2	35.0	36.1	36.6	32.6	36.9	25.6	33.9
	0.02	14.0	13.0	13.4	10.4	9.5	7.2	5.5	10.9
	0.03	1.9	1.2	1.6	0.7	1.0	0.2	0.4	1.1

tall, thin subjects often had rightward QRS axes. Simonson and Keys[8] noted a pronounced shift to the left of the QRS axis between their young group of men (eighteen through twenty-five years of age) and their older group of men (forty-five through fifty-five years of age). The mean for the younger group was +66.75 degrees whereas the mean for the latter was +37.77 degrees. By selecting subjects with normal bodily proportions, these authors determined that this leftward shift of the QRS axis with age occurred independently of body weight. However, they noted that body weight could be an additional factor causing leftward rotation of the QRS vector, particularly in their older age group. In this age group the QRS axis mean for extremely underweight subjects was +61.61 degrees, whereas the mean axis for markedly overweight subjects was +31.42 degrees. The effect of weight on QRS axis was not nearly so striking in the younger group of men studied by these authors. Statistical analysis of QRS axis, age, body weight and QRS amplitude in our study is given subsequently.

QRS Transition: The transition of the QRS complex in the precordial leads was determined on all tracings and the percentage distribution of these data by age group is given in Table XVII. It is apparent that the marked change in QRS axis in the frontal plane with increasing age is not accompanied by significant variation of the QRS axis in the transverse plane. Most transitions were at lead V_2, V_3 or V_4, with lead V_3 the most common. Sokolow and Friedlander[15] noted QRS transitions in leads V_2 through V_6 in their series of 150 subjects, leads V_3 and V_4 being the most common. Our data are roughly comparable; however, lead V_2 was more frequent than lead V_4 in our series. The concept that vertical QRS axes are associated with QRS transitions at lead V_5 or V_6, and that horizontal QRS axes are associated with transitions at lead V_1 or V_2 was not substantiated in our study. QRS

transitions in the transverse plane were random with respect to the QRS axis in the frontal plane. Furthermore, the trend toward leftward rotation of the QRS axis in the frontal plane in the older age groups was not associated with any change in the frequency of transitions at the various precordial positions.

Q Waves in Limb Leads: The presence or absence of Q waves in the limb leads, their duration and amplitude were determined for leads I, II, III, aVL and aVF (Table XVIII). They were not determined in the precordial leads because of their relatively small size. Q waves were found with increasing frequency beginning with lead aVL and proceeding clockwise to lead III. The range of duration for all leads was 0.01 through 0.03 second with the exception of lead III, for which there were ten records with Q waves with 0.04 second duration. The Q_3 problem has received considerable attention in the literature and is frequently a source of suspicion and confusion in clinical practice. The problem is one of distinguishing large Q waves in leads III and aVF resulting from a myocardial infarction of the inferior wall from similar Q waves in the absence of disease. The latter are often attributed to variations of cardiac position, but are actually caused by a disproportion of the standard electrocardiographic lead reference system to the particular body configuration of the subject. To investigate the Q_3 problem, the concurrent Q waves in leads II and aVF in those tracings with 0.03 and 0.04 second Q waves in lead III were tabulated (Table XIX). Of the ten tracings with a Q wave of 0.04 second duration in lead III, three had no Q waves in leads aVF and II, one had a Q wave of 0.02 second in lead aVF but none in lead II, and six had a Q wave equal to or greater than 0.02 second in lead aVF and equal to or greater than 0.01 second in lead II. This latter group constituted only 0.1

TABLE XIX
Incidence of Q Waves in Lead aVF and Lead II in the Presence of 0.03 and 0.04 Second Q_3

Duration (sec.) of Simultaneous Q Waves in Lead			No. of Subjects	Per Cent of Total Series
III	aVF	II		
0.03	0.0	0.0	62	1.03
0.04	0.0	0.0	3	0.05
0.03	≥0.02	0.0	5	0.08
0.04	≥0.02	0.0	1	0.02
0.03	≥0.02	≥0.01	136	2.26
0.04	≥0.02	≥0.01	6	0.10

TABLE XX
Incidence of Q Waves in Standard Limb Leads at Various QRS Axes*

QRS Axis in Frontal Plane (degrees)	Number of Persons With Q Wave in Lead				
	I	II	III	aVL	aVF
−75	1	...	...	1	...
−60	2	...	...	2	...
−45	16	...	...	19	...
−30	35	2	1	40	2
−15	79	4	...	85	1
0	145	30	5	142	14
+15	198	74	18	191	51
+30	259	141	80	245	95
+45	401	458	367	289	394
+60	289	553	523	140	530
+75	246	1,159	1,172	50	1,177
+90	13	377	414	9	399
+105	1	80	95	...	93
+120	...	1	2	...	1
Indeterminate	5	3	6	6	4
Total no. of Q waves, all axes	1,690	2,882	2,683	1,219	2,761

* There was no apparent variation among age groups.

TABLE XXI

Q Wave Amplitude in Leads I, II, III, aVL and aVF
Percentage Distribution of Entire Series*

Q Wave Amplitude (mv.)	I	II	III	aVL	aVF
None	71.9	52.1	55.4	79.7	54.1
0.05	22.7	31.3	21.7	15.1	28.7
0.10	4.5	10.6	11.9	3.9	11.2
0.15	0.8	3.7	5.3	0.8	3.6
0.20	0.2	1.6	3.4	0.5	1.4
0.25	0.0	0.5	1.0	0.1	0.5
0.30	0.1	0.2	0.8	0.0	0.2
0.35	0.0	0.1	0.3	0.0	0.0
0.40	0.0	0.0	0.1	0.0	0.1
0.45	0.0	0.0	0.1	0.0	0.0
0.50	0.0	0.0	0.1	0.0	0.0

* There was no apparent variation among age groups.

TABLE XXII

Terminal QRS Vector
Percentage of Each Age Group with S_1S_2 and $S_1S_2S_3$ Patterns

Age Group (yr.)	Terminal QRS Vector	
	S_1 S_2 Pattern	S_1 S_2 S_3 Pattern
<20	20.1	25.3
20–24	18.5	27.7
25–29	16.4	23.1
30–34	15.6	25.0
35–39	11.2	23.0
40–44	12.9	20.1
45 and >	7.7	21.0
All	15.3	23.8

per cent of the entire population surveyed and their normality might be viewed with some suspicion. However, these criteria alone were not utilized for the diagnosis of myocardial infarction of the inferior wall and a discussion of this point may be found in a previous paper in this series.[18] As expected, there were a large number of tracings (136) with Q waves of 0.03 second duration in lead III associated with a Q wave 0.02 second or greater in lead aVF and 0.01 second or greater in lead II. It is of importance to note that no tracing showed a Q wave of 0.05 second in any limb lead (except aVR).

A comparison of the occurrence of Q waves to the QRS axis appears in Table XX. Q waves in leads I and aVL were most frequently associated with a QRS axis of +45 degrees. Q waves in leads II, III and aVF occurred most often with a QRS axis of +75 degrees. Of interest is the relatively large number of Q waves in leads I and aVL and the rarity of Q waves in the other leads associated with horizontal axes (zero and −15 degrees). For instance, there were only five tracings with a Q wave in lead III when the QRS axis was zero degrees as compared to 145 in lead I and 142 in lead aVL. No tracing demonstrated a Q wave in lead III when the QRS axis was −15 degrees whereas there were seventy-nine tracings with Q waves in lead I and eighty-five in lead aVL. A Q wave of benign significance is often produced by brief initial forces of ventricular activation directed opposite to the main vector; for this reason Q waves in leads II, III and aVF will be associated with vertical axes and Q waves in leads I and aVL will be associated with horizontal axes. These factors and the trend toward leftward rotation of the QRS axis with age undoubtedly explain the increased incidence of Q waves in lead I with advancing age (Table XVIII).

Table XXI gives the percentage distribution of Q wave amplitude for the various leads assessed. These figures are in agreement with both Stewart and Manning[1] and Graybiel et al.[2] No attempt was made in our study to determine the ratio of Q wave amplitude to the largest R wave amplitude in any bipolar lead as many investigators have previously done. The ratio of Q to R waves was not considered important.

Terminal QRS Vector: On occasion considerable significance is attached to the presence of terminal negative waves in the QRS complexes of the standard bipolar limb leads. This has been variously called the $S_1S_2S_3$ pattern, delay in activation over the right ventricle and/or variation of intraventricular conduction. In order to determine the incidence of this pattern, the number of subjects in each age group with terminal $S_1S_2S_3$ and also those with just S_1S_2 were noted (Table XXII). In general, one-fourth to one-fifth of all subjects in each age group had a terminal negative wave in leads I, II and III. In addition, between 8 and 20 per cent of subjects in each age group had a terminal S wave in leads I and II but not in lead III. The incidence of the $S_1S_2S_3$ pattern decreased slightly with age (25 per cent in first age group and 21 per cent of last age group)

TABLE XXIII
Ratio of R to S Wave Amplitude in Leads V_1 and V_2
Percentage of Each Age Group With Ratio Greater Than 1

Age Group (yr.)	R/S Equal to or Greater Than 1 in Lead	
	V_1	V_2
<20	1.1	6.1
20–24	1.3	7.1
25–29	0.9	9.2
30–34	0.4	10.1
35–39	0.1	1.0
40–44	0.4	8.1
45 and >	0.2	10.4
All	0.7	8.5

but the S_1S_2 pattern changed considerably with age (20 per cent in the first group and 8 per cent in the last).

Both patterns are dependent on a terminal vector directed to the right. The $S_1S_2S_3$ pattern further limits the orientation of the terminal QRS vector toward the right shoulder. The terminal rightward vector may cause an R′ wave in lead V_1 particularly in $S_1S_2S_3$. This may be produced when the precordial electrodes are above the point of origin for the terminal vector. A common technical error is placing the electrodes in the third intercostal space. This will create a terminal R′ wave in lead V_2 as a technical artifact. This results in the erroneous diagnosis of incomplete right bundle branch block. A precordial map will clearly demonstrate the influence of precordial electrode placement in creating R′ waves in the presence of $S_1S_2S_3$ pattern.

In some subjects the anatomic relation of the fourth intercostal space to the heart results in the same picture. Finally, but far less commonly, the terminal QRS vector may be directed within the positive zone of lead V_1 resulting in a bonafide R′ wave. This does not necessarily mean that the terminal QRS vector is anterior. When it is anterior an R′ wave should also be noted in lead V_2. In our series an R′ wave was noted in lead V_1 in a small number of cases. Comparison of the incidence of these rightward terminal QRS forces to the height, weight, QRS duration and duration of R and S waves in lead V_2 was made, but no relation was observed.

Ratio of R/S Amplitude in Leads V_1 and V_2: Clinical significance is sometimes attached to an increase of the R/S amplitude ratio in leads V_1 and V_2. To assess the frequency of this finding the number of records in each age group with an R/S amplitude ratio of 1 or more in lead V_1 or V_2 was determined (Table XXIII). The finding of an R/S amplitude ratio of 1 or more in lead V_1 was relatively rare, less than 1 per cent of the entire series. A ratio of 1 or more was less rare in lead V_2 being as frequent as 10 per cent of some of the age groups. These statistics are roughly comparable to those of Sokolow and Friedlander,[15] who described a range of the R/S amplitude ratio in lead V_1 of zero through 1, and a range in lead V_2 of 0.1 through 13. An attempt to relate the occurrence of R/S amplitude ratios of greater than 1 in lead V_1 or V_2 to height, weight or heart rate was unrevealing.

TABLE XXIV
T Axis in Frontal Plane
Percentage Distribution by Age Group

T Axis in Frontal Plane (degrees)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
−15	0.1	0.1	0.2	0.8	1.1	1.0	0.2	0.5
0	1.9	2.4	2.6	6.1	3.4	3.5	4.0	3.3
+15	4.1	13.6	19.0	17.1	20.3	19.0	18.8	15.4
+30	15.9	14.5	11.0	17.3	16.5	14.7	15.7	15.0
+45	42.5	49.9	47.2	44.6	43.1	48.2	44.6	45.7
+60	22.6	11.2	7.9	6.2	7.3	6.8	8.8	10.6
+75	12.6	8.3	12.0	7.9	8.2	6.8	7.9	9.3
+90	0.3	...	0.1	...	0.1	...	...	0.1

T WAVE

T Axis in the Frontal Plane: The axis of the T vector was determined by using the standard hexaxial reference system; the results are shown in Table XXIV and Figure 5. The range was −15 through +90 degrees with few subjects at the extremes. The mode was +45 degrees. There appeared to be some leftward rotation of the T vector in the frontal plane with increasing age, which, although definite, was not as marked as the corresponding leftward shift of the QRS vector. In the first age group, 22.6 per cent of subjects had a T axis of +60 degrees, whereas only 8.8 per cent of the oldest age group did; correspondingly, only 4.1 per cent of the first age group had a T axis of +15 degrees, whereas 18.8 per cent of the last age group did. In their follow up of 1,000 Naval aviators, Packard et al.[7] noted that the mean T wave vector shifted only 1.9 degrees and maintained approximately the same range. Simonson and Keys[8] noted a more pronounced shift of the T vector between their younger group and their older group, from +42.78 to +32.87 degrees. Their statistics indicate that a shift of the T vector to the left may be associated with either increasing age or relative obesity, and that both factors may be additive in older obese subjects.

T Transition: The T transition in the precordial leads was determined for each subject. It was found that 99.7 per cent of the entire series had a T transition at or near lead V_1. The transition was considered to be at lead V_1 when all precordial T waves were upright if the T wave in lead V_1 was of less amplitude than the T of lead V_6. The remaining 0.3 per cent had T transitions at lead V_2 (inverted T in lead V_1 with flat or biphasic T in lead V_2), or at lead V_7 (progressively decreasing T wave amplitude in leads V_1 through V_6). This would indicate that regardless of whatever changes may occur in the T vector in the frontal plane with increasing age, this change is not of a nature to affect the configuration and transition of the T wave in the transverse plane.

Mean Spatial QRS-T Angle: The mean spatial QRS-T angle was calculated from a chart previously published.[16] The percentage frequency distribution by age group is shown in Table XXV. Table XXVI gives the quartiles. The range was zero through 139 degrees with few tracings with spatial angles above 70 degrees. Tracings with T wave changes often produce wide spatial QRS-T angles. However, all

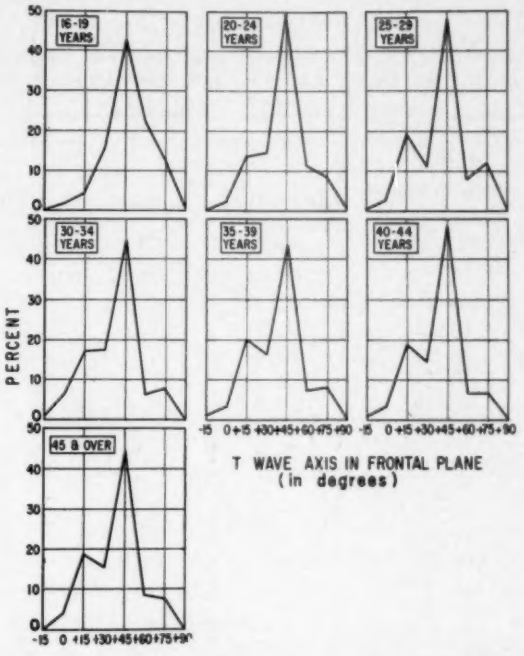


FIG. 5. Percentage distribution of T axis in the frontal plane within age groups.

electrocardiograms with any T wave abnormality were excluded from the study. There was extremely little variation with age due to the concomitant shift of the two vectors comprising the spatial QRS-T angle. Both the QRS and T vectors rotated leftward in the frontal plane with increasing age without a notable change in the transverse plane. It has been reported[17] that the spatial QRS-T angle rarely exceeds 50 degrees in the healthy person. This statement is not borne out by our data, as there were approximately 18 per cent in the entire series who had angles of 50 degrees or above. A more accurate estimate of the upper limits of normal might be 70 degrees, which would include 96 per cent of our series.

Comparisons of the spatial QRS-T angle were made to the height, weight, age, body build and heart rate of the subjects, but no relationship or trend could be established. Comparison of the spatial angle to the QRS axis indicated that the wider angles were usually associated with leftward rotation of the QRS axis.

S-T SEGMENT

Vector in the Frontal Plane: An elevation of the S-T segment above the T-P baseline was considered an electrical force for which the vector was determined. Of the 6,014 subjects 1,460 had a detectable S-T segment force. The percentage distribution of the detectable

TABLE XXV
Spatial QRS-T Angle
Percentage Distribution by Age Group

Spatial QRS-T Angle (degrees)	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
0–9	2.3	2.5	4.3	3.6	3.3	2.7	5.1	3.3
10–19	14.1	12.0	13.4	13.5	13.7	14.8	12.1	13.4
20–29	22.4	19.5	19.1	22.2	22.8	23.7	22.1	21.6
30–39	24.7	23.2	24.8	19.0	23.1	21.1	19.9	22.6
40–49	19.8	20.4	19.8	22.4	19.8	19.1	20.1	20.2
50–59	6.9	10.0	8.1	8.4	6.0	7.0	7.1	7.6
60–69	5.3	7.0	6.5	6.4	6.0	5.2	6.6	6.1
70–79	2.5	1.9	1.7	2.1	1.9	2.9	3.5	2.3
80–89	0.6	0.8	0.5	1.0	1.4	1.2	1.1	0.9
90–99	0.6	0.9	0.8	1.1	0.7	1.2	0.9	0.8
100–109	0.1	0.2	...	...	0.2	0.1	0.5	0.1
110–119	...	...	...	...	0.0	0.1	0.0	}
120–129	...	...	...	...	0.1	0.1	0.2	} 0.1
130–139	...	...	...	...	...	...	0.2	}
Indeterminate	0.8	1.6	1.0	0.4	0.9	0.6	0.5	0.9

S-T segment vectors is given in Table XXVII. The majority fell between +60 and +90 degrees. There was a slight decrease in the frequency of S-T segment forces in the older age group; 25 per cent of the first age group had notable S-T segment elevation, whereas only 15 per cent of the oldest age group did.

The statistics relative to S-T segment elevation given by Stewart and Manning[1] are not directly comparable to ours as the former were based on individual leads rather than vector magnitudes. However, the two series correspond in general. Graybiel et al.[2] found 85 per cent of 1,000 subjects had S-T segment elevation in lead I, 89 per cent in lead II and 46 per cent in lead III, considerably more than found in our study. The differences can probably be explained by differences in definition, and it is only important to realize that most investigators are aware of slight S-T segment elevation in many limb leads, particularly II, III and aVF which is not indicative of myocardial injury and is frequently found in normal people. The configuration of elevated S-T segments in our tracings was usually concave upwards when an S-T segment immediately followed the R wave of the QRS complex, but was convex upward if the S-T segment followed an S wave. In almost all cases the directions of the S-T segment and the T wave were parallel.

Greatest S-T Segment Amplitude in the Frontal Plane: When a detectable S-T segment force was noted the greatest amplitude of this force above the T-P baseline was calculated. The

TABLE XXVI
Spatial QRS-T Angle
Quartiles by Age Group*

Quartile	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
First	22	23	22	24	23	23	24	23
Second	33	36	35	35	35	35	35	35
Third	47	47	47	47	45	45	47	46

* All figures shown are in degrees.

TABLE XXVII

S-T Segment Vector in Frontal Plane
Percentage Distribution of Entire Series and of Those with an S-T Segment Vector

S-T Segment Vector in Frontal Plane (degrees)	Per Cent of Entire Series	Per Cent of Those with an S-T Segment Vector
None	75.5	...
−45	0.1	0.6
−30	0.1	0.6
−15	0.1	0.6
0	1.6	6.7
+15	0.1	0.2
+30	0.3	1.3
+45	0.7	2.8
+60	5.1	20.6
+75	5.9	23.9
+90	9.8	40.0
+105	0.6	2.4
+120	0.1	0.4

TABLE XXVIII

Greatest S-T Segment Amplitude in Frontal Plane
Percentage Distribution of Entire Series and of Those with an S-T Segment Vector

Greatest S-T Segment Amplitude in Frontal Plane (mv.)	Per Cent of Entire Series	Per Cent of Those with an S-T Segment Vector
None	75.5	...
0.05	16.4	66.8
0.10	7.2	29.5
0.15	0.7	2.9
0.20–0.25	0.2	0.8

results of this are shown in Table XXVIII as a composite for the entire series. There was no appreciable variation with age with the exception of the first and second age groups; 15 per cent of the first age group and 12 per cent of the second age group had S-T segment elevation of 0.10 and 0.15 mv., respectively, whereas only 3 per cent of the last age group had elevations of this size. In the intermediate groups approximately 5 per cent had these elevations. S-T segment elevation is not only more frequent in young adults, but is also of greater magnitude when present. Although precise delineation of this portion of the electrocardiogram is not essential in ordinary practice, it may be helpful to recognize that S-T segment elevation as great as 0.3 or 0.4 mv. may occur in the absence of disease.

S-T Segment in the Precordial Leads: The presence of S-T segment elevation above the T-P baseline in the precordial leads was determined. All tracings were categorized into one of five groups as follows: group 1, anterior S-T segment force (elevation in leads V_2, V_3 and V_3); group 2, lateral S-T segment force (elevation in leads V_3 through V_6); group 3, rightward S-T segment force (elevation in leads V_1 and V_2 only); group 4, anterolateral S-T segment force (elevation in all precordial leads); and group 5, no S-T segment elevation in any precordial lead.

Table XXIX provides the results of this analysis. S-T segment elevation in the precordial leads without acute injury is well recognized, but it

TABLE XXIX

S-T Segment Elevation in the Precordial Leads
Percentage Distribution by Age Group

S-T Segment Vector in Transverse Plane Directed	Age Group (yr.)							
	<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
Anterior (elevation in leads V_2, V_3, V_4)	38.3	38.2	42.2	47.3	51.0	45.6	47.4	43.8
Lateral (elevation in leads V_3, V_4, V_5, V_6)	30.3	30.8	30.0	22.2	19.1	21.9	15.5	24.0
Rightward (elevation in leads V_1, V_2 only)	6.7	5.2	7.5	7.4	6.9	5.7	8.2	6.8
Anterolateral (elevation in all precordial leads)	21.3	23.0	20.4	13.2	10.7	13.5	10.9	16.8
No elevation in any precordial lead	3.4	2.7	7.3	9.9	12.3	13.4	17.9	8.8

TABLE XXX
Greatest S-T Segment Elevation in Precordial Leads
Percentage Distribution of Entire Series

Greatest S-T Segment Elevation in Precordial Leads (mv.)	Per Cent
None	8.8
0.1	44.3
0.2	38.4
0.3	7.9
0.4	0.5
0.5	0.1

is of interest to note the common occurrence of this phenomenon. Only 8.8 per cent of the entire survey showed no S-T segment elevation in any precordial lead. Inspection of Table XXIX indicates a slight trend towards anterior S-T segment forces with increasing age at the expense of lateral and anterolateral forces. It may also be noted that there is a considerably higher percentage in the older age groups with no S-T segment elevation in any precordial lead as compared to the younger age groups.

The magnitude of the S-T segment forces in the precordial leads was also assessed and the percentage distribution of these data is given in Table XXX. The value recorded was the largest observed in any precordial lead. S-T segment elevation of this non-specific variety was of much greater amplitude in the younger age groups. In the first age group 15 per cent had elevation of 0.3 mv. whereas only 3 per cent of the last age group did; 55 per cent of the first age group had elevation of 0.2 mv. compared to only 24 per cent of the last age group. Sokolow and Friedlander[15] found that S-T segment elevation up to 3 mm. was not uncommon in leads V_1, V_2 and V_3, but rarely exceeded 1 mm. in leads V_4 through V_6. In general, our

TABLE XXXI
QRS Amplitude in Leads I, aVF, V_2 and V_6
Percentage Distribution by Age Group

Lead	QRS Amplitude (mv.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I	0.00–0.15	0.5	0.1	0.3	...	...	0.1	...	0.2
	0.20–0.35	4.7	8.1	5.2	4.7	3.3	4.3	5.3	5.1
	0.40–0.55	26.9	27.0	25.1	17.3	21.6	18.1	18.3	22.6
	0.60–0.75	29.8	28.0	27.5	30.3	28.5	27.2	27.8	28.5
	0.80–0.95	22.7	18.7	23.1	23.3	20.0	21.2	22.1	21.6
	1.00–1.15	10.1	11.0	11.1	15.2	15.9	16.4	14.4	13.2
	1.20–1.35	3.2	4.5	4.8	5.7	5.6	7.3	7.3	5.3
	1.40–1.55	1.4	1.8	1.8	2.3	3.4	3.7	3.8	2.5
	1.60–1.75	0.4	0.4	0.5	0.7	1.1	1.1	0.5	0.7
	1.80–1.95	0.3	0.0	0.3	0.4	0.4	0.2	0.4	0.3
	2.00–2.15	...	0.4	0.2	0.1	...	0.1	...	0.1
aVF	0.00–0.15	0.4	0.1	0.1	0.4	0.3	0.5	0.5	0.3
	0.20–0.35	0.2	1.5	2.8	5.0	8.5	10.2	15.5	5.4
	0.40–0.55	1.7	6.0	9.2	16.0	16.9	20.2	26.0	12.5
	0.60–0.75	7.1	11.7	17.8	21.8	23.6	25.5	25.2	18.1
	0.80–0.95	12.6	16.6	18.5	20.6	17.9	19.5	14.1	17.1
	1.00–1.15	17.2	18.5	15.0	15.6	13.8	12.0	8.4	14.8
	1.20–1.35	13.8	14.4	11.7	9.3	10.5	5.5	4.9	10.5
	1.40–1.55	14.9	9.6	11.1	6.2	4.4	3.5	3.3	8.1
	1.60–1.75	13.8	8.8	6.4	2.1	2.4	1.9	1.3	5.8
	1.80–1.95	7.2	5.9	4.3	1.5	0.8	0.6	0.5	3.3
	2.00–2.15	5.4	3.9	1.6	0.8	0.4	0.5	0.0	2.1
	2.20–2.35	3.1	1.6	0.8	0.4	0.0	0.1	0.0	1.0
	2.40–2.55	1.8	0.9	0.6	0.1	0.1	...	0.2	0.6
	2.60–2.75	0.6	0.4	0.1	0.0	0.1	...	...	0.2
	2.80–2.95	0.1	0.1	...	0.2	...	...	...	0.1

TABLE XXXI (*Continued*)

Lead	QRS Amplitude (mv.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
V_2	0.20–0.35	...	...	...	...	...	0.1	...	0.2
	0.40–0.55	...	...	0.1	0.2	0.4	0.0	0.9	
	0.60–0.75	...	0.3	0.4	1.1	1.1	0.9	2.0	0.7
	0.80–0.95	0.6	0.8	1.5	2.7	3.4	4.6	5.9	2.5
	1.00–1.15	1.0	1.8	2.9	5.2	5.8	6.2	9.9	4.2
	1.20–1.35	1.6	4.5	7.6	7.3	8.9	9.4	11.3	6.8
	1.40–1.55	3.0	4.8	8.7	12.1	12.2	13.0	12.2	9.0
	1.60–1.75	5.5	8.3	9.8	11.2	11.7	13.2	13.9	10.1
	1.80–1.95	7.8	9.5	9.4	12.6	13.6	16.4	14.4	11.6
	2.00–2.15	7.8	9.5	12.1	12.4	12.8	13.3	10.6	11.1
	2.20–2.35	9.6	11.7	9.9	10.1	8.3	8.6	7.1	9.5
	2.40–2.55	9.7	12.0	10.4	9.6	8.3	5.7	3.7	8.9
	2.60–2.75	11.2	10.5	7.9	6.1	5.1	2.9	2.9	7.1
	2.80–2.95	9.9	5.8	5.5	3.8	2.5	3.0	2.0	5.0
	3.00–3.15	7.6	6.2	5.2	2.3	2.3	1.1	1.3	4.1
	3.20–3.35	7.3	2.9	3.2	2.1	1.2	1.0	1.3	3.0
	3.40–3.55	5.1	4.7	2.5	0.8	0.8	0.5	0.2	2.3
	3.60–3.75	4.2	2.3	1.4	0.2	0.7	0.1	0.2	1.5
	3.80–3.95	2.9	1.7	0.4	0.0	0.2	...	0.0	0.9
	4.00–4.15	2.4	1.4	0.6	0.1	0.2	...	0.0	0.8
	4.20–4.35	1.4	0.4	0.1	0.1	0.0	...	0.0	0.3
	4.40–4.55	0.6	0.6	0.1	0.1	0.1	...	0.2	0.3
	4.60–4.75	0.3	0.2	0.0	...	0.1	...	...	0.1
	4.80–4.95	0.1	...	0.1	...	...	...	...	0.1
	5.00 and >	...	...	...	...	...	...	...	
V_6	0.20–0.35	...	...	...	...	0.2	...	0.4	0.1
	0.40–0.55	0.5	1.2	1.0	0.7	1.0	2.0	3.3	1.2
	0.60–0.75	2.8	3.4	4.9	5.5	5.1	6.5	11.0	5.2
	0.80–0.95	7.0	6.6	8.6	10.5	14.6	12.9	16.1	10.4
	1.00–1.15	11.5	12.9	18.6	21.1	19.3	20.2	16.1	16.9
	1.20–1.35	20.0	18.5	17.5	20.7	21.0	19.5	18.8	19.5
	1.40–1.55	17.0	17.5	16.8	15.2	14.3	15.9	14.4	16.0
	1.60–1.75	16.2	14.6	13.0	11.3	11.2	9.8	8.2	12.5
	1.80–1.95	10.1	10.1	9.0	6.1	6.6	5.7	5.1	7.8
	2.00–2.15	7.5	6.9	5.3	5.3	3.4	4.0	4.6	5.4
	2.20–2.35	3.2	4.3	2.1	1.8	1.9	1.5	1.1	2.4
	2.40–2.55	2.0	1.8	1.5	0.8	0.6	0.7	0.7	1.2
	2.60–2.75	1.1	1.3	1.1	0.6	0.2	0.4	0.2	0.7
	2.80–2.95	0.6	0.5	0.4	0.2	0.3	0.7	...	0.4
	3.00–3.15	0.3	0.2	0.1	0.1	0.0	0.1	...	0.1
	3.20–3.35	0.1	0.2	0.2	...	0.2	...	...	0.1

statistics are in agreement with these findings as our larger amplitudes were usually found in the anteriorly located leads (V_2 and V_3).

True S-T segment depression of plateau nature was considered a cause for exclusion of the record from this study. Junctional S-T segment changes were frequently observed, not numerically assessed.

QRS AMPLITUDE

The QRS complex, regardless of its configuration or the lead in which it is observed, is a graphic record of the electrical events of ventricular activation. Differences in the shape of this complex from one lead to the next are purely a function of the geometric relation of that lead to the electrical field. All electrocardiographic leads record coordinate values, and whether the deflection is positive or negative in a given lead does not have any bearing on its total amplitude. For these reasons, the measurements of QRS amplitude in this series were made from the most positive to the most negative point of the QRS complex, that is, from the

TABLE XXXII
QRS Amplitude in Leads I, aVF, V_2 and V_6
Quartiles by Age Group*

Lead	Quartile	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I	First	0.50	0.50	0.55	0.60	0.60	0.60	0.60	0.55
	Second	0.70	0.70	0.70	0.75	0.75	0.80	0.75	0.75
	Third	0.90	0.90	0.90	0.95	1.00	1.00	1.00	0.95
aVF	First	1.00	0.85	0.75	0.60	0.55	0.50	0.45	0.65
	Second	1.35	1.10	1.00	0.80	0.80	0.70	0.65	0.95
	Third	1.70	1.50	1.35	1.10	1.00	0.95	0.90	1.30
V_2	First	2.10	1.85	1.65	1.50	1.50	1.40	1.30	1.60
	Second	2.60	2.35	2.10	1.90	1.85	1.80	1.70	2.05
	Third	3.15	2.80	2.60	2.40	2.30	2.15	2.05	2.60
V_6	First	1.20	1.20	1.10	1.05	1.00	1.00	0.90	1.50
	Second	1.50	1.45	1.35	1.30	1.25	1.25	1.20	1.35
	Third	1.80	1.80	1.70	1.60	1.55	1.55	1.50	1.65

* All figures shown are in millivolts.

peak of the R wave, if present, to the nadir of the S wave, if present. All measurements were made to the nearest 0.05 mv. Leads I, aVF and V_2 were selected as most nearly representing mutually perpendicular coordinates. Leads I and V_6 both approximate an X coordinate and thus both were measured; lead aVF approximates a Y coordinate and lead V_2 a Z coordinate. The percentage distributions of QRS amplitudes in individual leads are shown in Table XXXI and Table XXXII provides the quartiles. Figure 6 illustrates the differences between age groups in the distributions of QRS amplitudes in the four leads by showing the cumulative per cent distributions for the sixteen- to twenty-year, thirty- to thirty-four-year and forty-five-year and over age groups.* The distribution of the QRS amplitude in lead I was similar for the seven age groups, whereas the distribution of the QRS amplitude in leads aVF and V_2 decreased with each older age group. If a simple geometric shift of the vector with age were the only factor responsible for these observed changes, the QRS amplitude in lead I would increase significantly as the amplitude in lead aVF diminishes. The fact that amplitude is considerably lower in such a high per cent of the subjects in the older age groups for both leads aVF and V_2, whereas the amplitude is not significantly changed in lead I means that the measurable magnitude of the spatial QRS vector is progressively diminished in the older age groups.

Plane and Spatial Measurements: Considering the QRS complex as representing a spatial electrical event, and therefore not having peculiar significance in one lead as compared to another, an attempt was made to find a measurement related to the QRS voltage in the frontal and transverse planes and spatially. This was accomplished by utilizing the QRS amplitudes in the coordinate leads which define the planes. One measurement for the frontal plane was the sum of the QRS amplitude in leads I + aVF. Another measurement was obtained by using the principle of the Pythagorean theorem, $\sqrt{I^2 + (aVF)^2}$. For the transverse plane the sum of the QRS amplitudes in leads V_2 and V_6 was calculated. A measurement related to ventricular excitation expressed spatially was obtained from the sum of the QRS amplitudes in leads I, aVF and V_2 and in leads V_6, aVF and V_2. The latter two methods differ in relation to the extent that leads V_6 and I are not in-

* The cumulative per cent is the per cent of subjects in a group that have a given measured value or less. As an illustration, in Figure 6 (solid line), 20 per cent of the group had a voltage of 0.95 mv. or less and 80 per cent had a voltage of 1.75 mv. or less.

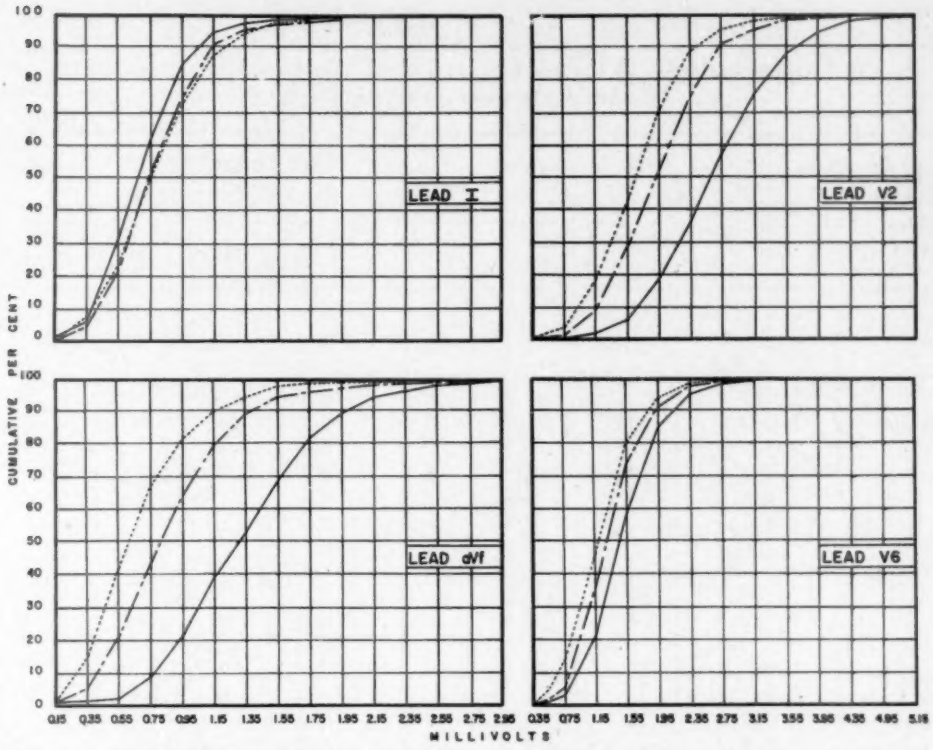


FIG. 6. Cumulative percentage distributions of QRS amplitude for the sixteen- to nineteen-year group (solid line), thirty- to thirty-four–year group (dash-dot line), and forty-five years and over group (broken line). QRS amplitude was measured from the highest to the lowest deflection, not as individual R or S waves. Note the decrease in measurable voltage with each older age group in leads aVF, V_2 and V_6, and the very minimal differences between the three age groups in lead I.

terchangeable as X coordinates. The frequency distributions for these values by age group are found in Table XXXIII and Table XXXIV provides the quartiles. Figure 7 displays the cumulative percentage of several of these mathematical calculations for the first, fourth and last age groups. Figure 8 gives the cumulative percentage for each of the seven age groups for the sum of leads I + aVF + V_2. There was a successively higher percentage of subjects with lower voltage values with each age group.

What these various curves demonstrate is that measurable voltage of ventricular excitation progressively decreases with older age groups when evaluated by technics of vector analysis utilizing planes and spatial measurements. This observation is important since measurements of this type may provide a basis for evaluating aging of the heart which cannot now be done with usual interpretation methods. The values for QRS amplitude expressed in terms of vector analysis may find other application in the clinical situation. Although there is nothing diagnostic about a QRS amplitude which is low when compared to normal values for a given age, this finding, when combined with the total clinical picture, may assume more importance. Conversely, a QRS amplitude which at first glance might appear high and be suggestive of hypertrophy (according to some criteria) may be well within the range of normal when values based on age are consulted.

Correlation coefficients between QRS amplitude, age, QRS axis and deviation of body weight from optimum weight are given in Table XXXV. A correlation coefficient provides a measure of relationship between two variables. In this discussion a coefficient of zero indicates no linear relationship. Values between zero and 1 quantitate the degree of relation. A negative correlation indicates that the two variables under comparison are inversely related. The QRS amplitude determinations of leads I + aVF, V_2 + V_6 and I + aVF + V_2 were utilized for this statistical analysis for it was thought that they represented the best index for assessing QRS amplitude in the frontal and transverse planes and spatially.

TABLE XXXIII

QRS Amplitude Measured in the Frontal and Transverse Planes and Spatially
Percentage Distribution by Age Group

Combinations of Amplitudes from Indicated Co-ordinate Leads	QRS Amplitude (mv.)	Age Group (yr.)							
		< 20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I + aVF (frontal plane)	0.0–0.4	0.2	...	0.1	...	...	0.1	...	0.1
	0.5–0.9	0.6	1.1	2.2	2.2	4.0	4.2	7.7	2.8
	1.0–1.4	8.4	18.6	23.3	31.6	34.2	38.5	45.3	26.7
	1.5–1.9	35.5	40.3	42.9	44.7	42.0	40.9	34.9	40.3
	2.0–2.4	34.1	25.6	22.0	17.0	16.5	13.8	10.6	21.1
	2.5–2.9	16.0	11.5	7.9	3.3	2.7	2.2	0.9	7.1
	3.0–3.4	4.4	2.3	1.5	1.0	0.6	0.2	0.5	1.7
	3.5–3.9	0.6	0.6	0.1	0.1	0.0	...	...	0.2
	4.0 and above	...	...	...	...	...	...	...	...
$\sqrt{I^2 + (aVF)^2}$ (frontal plane)	0.0–0.4	0.3	0.1	0.2	0.1	0.3	0.4	0.5	0.3
	0.5–0.9	5.4	11.7	17.8	22.2	27.2	29.9	37.7	20.1
	1.0–1.4	41.1	49.9	50.3	59.0	54.7	54.8	50.6	51.1
	1.5–1.9	37.7	28.5	25.9	16.1	16.1	13.5	10.4	22.5
	2.0–2.4	12.4	8.2	5.0	2.2	1.6	1.4	0.5	5.0
	2.5–2.9	3.0	1.5	0.8	0.2	0.0	...	0.2	0.9
	3.0 and above	0.0	0.1	...	0.1	0.1	...	...	0.1
$V_2 + V_6$ (transverse plane)	0.5–0.9	...	...	...	...	...	0.1	...	0.4
	1.0–1.4	...	...	0.2	0.4	0.4	0.5	1.8	
	1.5–1.9	0.6	1.7	1.3	2.9	3.3	5.7	8.6	3.0
	2.0–2.4	1.8	3.8	9.1	10.9	14.0	12.4	18.5	9.2
	2.5–2.9	6.9	11.2	14.9	23.4	22.4	26.2	25.8	17.7
	3.0–3.4	14.6	17.7	23.1	23.0	25.9	26.1	21.9	21.4
	3.5–3.9	18.8	22.4	20.6	17.8	18.5	15.9	13.5	18.6
	4.0–4.4	22.4	17.3	15.9	13.5	8.9	8.0	5.9	13.9
	4.5–4.9	16.1	13.7	8.5	5.3	4.0	3.4	2.6	8.3
	5.0–5.4	9.9	6.9	4.1	2.2	2.2	1.2	1.1	4.4
	5.5–5.9	4.8	3.1	1.2	0.5	0.2	0.4	0.4	1.7
	6.0–6.4	2.8	1.5	0.6	0.0	0.2	0.1	...	0.9
	6.5–6.9	0.8	0.5	0.2	0.1	...	...	...	0.3
	7.0 and above	0.4	0.1	0.2	...	...	...	...	0.1
I + aVF + V_2 (spatially)	1.0–1.4	...	...	...	...	0.1	0.2	0.7	0.1
	1.5–1.9	0.2	0.2	0.9	1.3	1.7	2.1	2.9	1.2
	2.0–2.4	0.5	1.8	2.9	5.8	7.2	8.7	15.0	5.2
	2.5–2.9	2.0	6.1	10.9	15.3	16.2	19.4	22.9	12.2
	3.0–3.4	7.8	13.3	17.0	24.5	23.9	27.1	26.0	19.0
	3.5–3.9	14.5	20.1	22.2	18.3	23.7	21.6	17.6	19.7
	4.0–4.4	17.1	20.6	17.8	17.1	14.3	11.6	8.0	15.8
	4.5–4.9	17.5	14.2	13.2	11.9	7.8	5.8	4.2	11.3
	5.0–5.4	16.9	10.2	8.0	3.4	3.3	2.1	1.6	7.2
	5.5–5.9	10.9	5.9	3.9	1.3	1.1	1.0	0.9	4.0
	6.0–6.4	7.3	4.1	1.9	0.6	0.4	0.4	0.2	2.5
	6.5–6.9	3.0	2.0	0.8	0.4	0.1	...	...	1.0
	7.0–7.4	1.3	1.4	0.3	0.0	0.2	...	...	0.5
	7.5–7.9	0.6	...	0.2	0.0	...	...	...	0.1
	8.0–8.4	0.3	...	...	0.0	...	...	...	0.1
	8.5–8.9	0.2	...	...	0.1	...	...	...	

TABLE XXXIII (*Continued*)

Combinations of Amplitudes from Indicated Coordinate Leads	QRS Amplitude (mv.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
$V_6 + aVF + V_2$ (spatially)	1.0–1.4	...	...	...	...	0.1	0.1	0.2	0.4
	1.5–1.9	...	...	...	0.1	0.7	0.5	2.2	
	2.0–2.4	0.2	1.1	1.2	2.2	2.9	4.3	7.3	2.4
	2.5–2.9	0.6	1.7	3.7	7.9	8.6	10.4	15.5	6.1
	3.0–3.4	1.9	4.7	8.6	16.1	17.3	18.8	21.4	11.7
	3.5–3.9	5.4	11.0	15.7	19.9	19.3	23.2	21.9	15.8
	4.0–4.4	12.6	14.3	18.1	16.0	20.6	20.0	14.6	16.6
	4.5–4.9	14.8	17.2	17.6	16.5	15.2	11.1	7.9	14.7
	5.0–5.4	14.9	17.0	14.3	10.2	7.5	6.1	4.9	11.3
	5.5–5.9	15.2	11.3	9.6	6.4	4.4	2.6	2.2	8.0
	6.0–6.4	13.1	8.3	5.3	3.0	1.9	1.6	1.5	5.5
	6.5–6.9	8.6	5.6	2.3	1.2	1.1	1.0	0.2	3.2
	7.0–7.4	6.0	4.8	2.5	0.1	0.2	0.2	0.0	2.3
	7.5–7.9	3.2	1.4	0.3	0.0	0.2	...	0.2	0.9
	8.0–8.4	2.2	0.9	0.4	0.2	...	...	...	0.6
	8.5–8.9	0.9	0.6	0.2	0.0	...	...	...	0.3
	9.0 and above	0.3	0.2	0.1	0.1	...	...	...	0.1

TABLE XXXIV

QRS Amplitude Measured in the Frontal and Transverse Planes and Spatially Quartiles by Age Groups

Combinations of Amplitudes from Indicated Coordinate Leads	Quartile	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I + aVF (frontal plane)	First	1.70	1.55	1.45	1.40	1.35	1.30	1.20	1.40
	Second	2.05	1.85	1.75	1.65	1.60	1.55	1.45	1.70
	Third	2.40	2.25	2.10	1.90	1.90	1.85	1.70	2.05
$\sqrt{I^2 + (aVF)^2}$ (frontal plane)	First	1.27	1.12	1.07	1.02	0.98	0.96	0.89	1.04
	Second	1.54	1.37	1.31	1.20	1.17	1.13	1.07	1.26
	Third	1.84	1.68	1.58	1.41	1.38	1.36	1.29	1.55
$V_2 + V_6$ (transverse plane)	First	3.5	3.2	2.9	2.7	2.6	2.6	2.4	2.8
	Second	4.1	3.8	3.5	3.2	3.1	3.0	2.8	3.4
	Third	4.7	4.5	4.1	3.8	3.7	3.5	3.4	4.1
$I + aVF + V_2$ (spatially)	First	4.00	3.59	3.30	3.05	2.99	2.86	2.64	3.17
	Second	4.73	4.20	3.91	3.58	3.52	3.36	3.16	3.81
	Third	5.46	4.95	4.62	4.29	4.08	3.90	3.71	4.58
$V_6 + aVF + V_2$ (spatially)	First	4.6	4.2	3.8	3.4	3.3	3.2	2.9	3.6
	Second	5.4	5.0	4.5	4.1	4.0	3.8	3.5	4.3
	Third	6.3	5.8	5.3	4.9	4.6	4.4	4.1	5.2

* All figures shown are in millivolts.

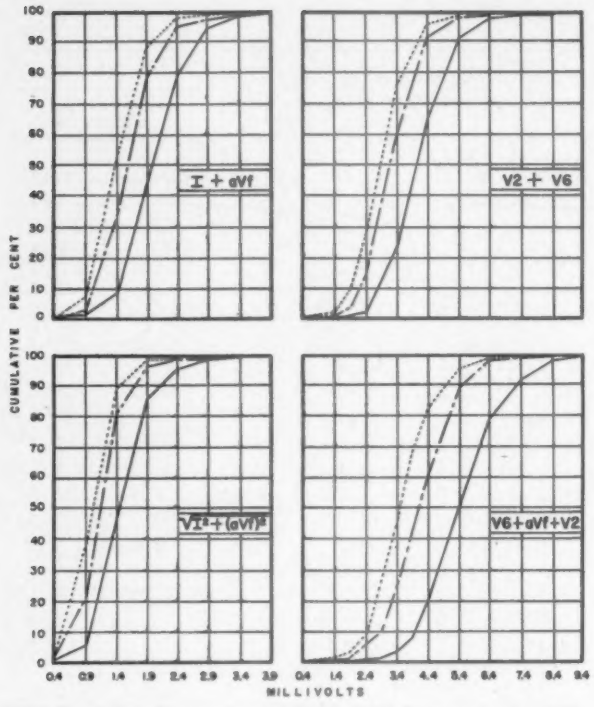


FIG. 7. Cumulative percentage distributions of QRS amplitude estimated for the frontal plane (leads I + aVF and $\sqrt{I^2 + (aVF)^2}$) transverse, plane (leads $V_2 + V_6$) and spatially (leads $V_6 + aVF + V_2$). Solid line, sixteen- to nineteen-year age group; dash-dot line, thirty- to thirty-four-year age group; broken line, forty-five years and over age group.

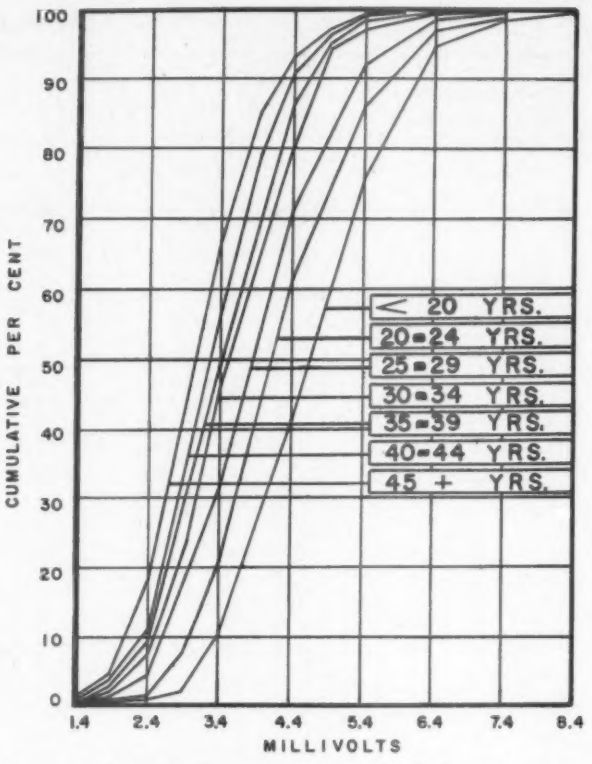


FIG. 8. Cumulative percentage distributions of the sum of the QRS amplitudes in leads I, aVF and V_2, representing measurable QRS voltage spatially. Note the decrease in voltage distribution with each older age group.

Inspection of Table XXXV reveals that the QRS amplitude, whether observed in the frontal or transverse planes or spatially, has an inverse relation to age or more simply stated, QRS amplitude tends to decrease with age on a group basis. The correlation coefficient for leads I + aVF, $V_2 + V_6$ and I + aVF + V_2 with age are −0.37, −0.42 and −0.47, respectively. QRS axis in the frontal plane was positively related to QRS amplitude, that is, the more vertical axes were associated with larger amplitudes and the more horizontal axes with lower amplitudes. QRS axis was inversely related to age; in other words the older age groups showed association with more leftward axes than did the younger age groups. Similarly, body weight was inversely related to QRS axis, that is, the overweight groups tended to be associated with leftward axes. These relations between two variables were determined without regard to the influence of the other two variables. Because these variables are undoubtedly interrelated, a measurement of the relation of two of the variables with the effect of the other variables under consideration held constant was accomplished with partial correlation coefficients.

TABLE XXXV

Correlation Coefficients Between the Indicated Variables

	Age	Axis	Weight*
Amplitude from leads			
I + aVF	−0.37	0.29	−0.18
$V_2 + V_6$	−0.42	0.25	−0.20
I + aVF + V_2	−0.47	0.34	−0.25
Age		−0.34	0.36
Axis			−0.33

* Weight is the difference between the number of pounds each individual weighed and the standard weight for his height for ages twenty-six to thirty years as defined in Air Force Manual 160-1.

Table XXXVI gives the partial correlation coefficients for the relation of QRS amplitude to age, QRS axis and body weight; and of QRS axis to age and body weight. In each instance the influence of the other two variables has been held constant and a more precise determination of the relation between the two variables under consideration was obtained. QRS amplitude is inversely related to age. It tends to decrease with age regardless of body weight or QRS axis. The partial correlation coefficients of QRS amplitude from leads I + aVF, $V_2 + V_6$ and I + aVF + V_2 with age are −0.30, −0.35 and −0.37, respectively. These are each

TABLE XXXVI

Partial Correlation Coefficients Between the Indicated Variables When the Effect of the Two in Parentheses is Removed

	Age (axis and weight)	Axis (age and weight)	Weight (axis and age)
Amplitude from leads			
I + aVF	−0.30	0.18	−0.00
$V_2 + V_6$	−0.35	0.11	−0.02
I + aVF + V_2	−0.37	0.20	−0.05

	Axis		Axis
Age (amplitude and weight) when amplitude is from leads		Weight* (amplitude and age) when amplitude is from leads	
I + aVF	−0.18	I + aVF	−0.23
$V_2 + V_6$	−0.19	$V_2 + V_6$	−0.23
I + aVF + V_2	−0.15	I + aVF + V_2	−0.22

* Weight is the difference between the number of pounds each subject weighed and the standard weight for his height for ages twenty-six to thirty years as defined in Air Force Manual 160-1.

somewhat lower than the values for the relationship of QRS amplitude to age when weight and axis were not considered (Table xxxv).

Of particular note is the extremely low partial correlation of body weight and QRS amplitude—it is practically zero. This implies that changes in body weight are not associated with changes in QRS amplitude after effects of age and axis have been taken into account. The relation of body weight to QRS axis, however, is not zero. The partial correlation coefficient for these two variables is −0.23, indicating that increase in body weight over optimum is associated with leftward rotation of the QRS axis. These correlation coefficients are significantly different from zero because of the large size of the subject population.

Conclusions Derived from Statistical Determinations: This series of statistical determinations was performed in an attempt to distinguish the interrelated effects of four variables on each other. The analyses and related discussion given here may be summarized for the group of subjects by the following general statements: (1) QRS amplitude whether considered in the frontal or transverse planes or three dimensionally tends to decrease from younger to older age groups regardless of the effect of QRS axis or body weight changes; (2) The QRS axis in the frontal plane shows a slight trend toward leftward rotation from younger to older age groups independent of QRS amplitude and body weight changes; (3) Increases in body weight above optimum were associated with leftward QRS axes; and (4) Body weight and QRS amplitude are not related.

Effect of Aging on QRS Voltage: These conclusions are not meant to imply cause and effect, as correlation coefficients do not provide information of this type. They merely quantitate the relation between variables. Some relations arise from mutual dependence of two variables on a third or fourth unknown factor. While these limitations are recognized, it does not seem unreasonable to postulate a cause and effect relationship for some of the observations in this study. Many of the effects of age on the myocardium are known and it is not inconceivable that progressive myocardial fibrosis, clinically undetectable coronary atherosclerosis and other degenerative changes can result in decreased voltage of ventricular excitation. In the same way, changes of the QRS axis might be produced.

Other factors which may be a direct result of age may influence voltage resulting from cellular excitation. The aging cell may behave differently electrically. The voltage across the wave front of excitation is dependent on the size and shape of the wave front and the density of charge on it. The density of charge can be affected by the control of sodium current effected on stimulation of the cell membrane and its action as a dielectric constant or electrical filter. If the amount of sodium flux diminishes, the potential difference across the wave front decreases. These factors which may be associated with aging are theoretical at present; however, the change in QRS amplitude in older age groups is not theoretical regardless of its cause. These observations suggest the possibility that QRS amplitude measurements may be important in a serial fashion in studying aging. The specific causes of all the factors related to the reason for these changes and their full significance will require longitudinal studies and additional experimental work.

The changes of QRS voltage and axis with age have

TABLE XXXVII
T Wave Amplitude in Leads I, aVF, V_2 and V_6
Percentage Distribution by Age Group

Lead	T Wave Amplitude (mv.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I	0.00–0.15	4.9	5.0	9.4	8.8	12.3	10.9	16.8	9.2
	0.20–0.35	71.5	72.5	69.5	72.5	73.8	75.8	72.9	72.5
	0.40–0.55	22.6	21.6	20.1	18.3	13.6	12.7	9.9	17 6
	0.60–0.75	1.0	0.9	1.0	0.4	0.3	0.6	0.4	0.7
aVF	0.00–0.15	11.6	18.4	23.4	30.1	33.2	35.5	37.5	25.8
	0.20–0.35	60.1	64.3	63.2	61.0	59.6	57.3	57.2	60.6
	0.40–0.55	26.2	16.3	13.2	8.5	7.0	7.1	5.3	12.9
	0.60–0.75	2.0	1.0	0.2	0.4	0.2	0.1	...	0.7
	0.80–0.95	0.1	...	...	0.1	...	...	...	
V_2	0.00–0.15	0.5	0.2	0.6	1.2	1.4	1.0	1.5	0.9
	0.20–0.35	7.4	6.3	9.5	10.3	13.2	12.0	14.4	10.1
	0.40–0.55	22.9	24.1	25.5	26.8	29.6	31.3	31.8	27.0
	0.60–0.75	27.3	31.7	30.7	32.7	32.6	31.9	31.4	31.0
	0.80–0.95	24.7	23.5	19.7	19.2	16.1	17.3	15.2	19.8
	1.00–1.15	11.1	9.3	9.7	7.5	5.2	5.0	4.4	7.8
	1.20–1.35	4.0	3.7	3.5	1.8	1.9	1.1	0.7	2.6
	1.40–1.55	1.8	0.9	0.5	0.4	0.1	0.2	0.4	0.7
	1.60–1.75	0.1	0.3	0.3	0.1	...	0.1	0.2	0.2
	1.80–1.95	0.2	...	...	...	...	...	...	
V_6	0.00–0.15	3.5	3.7	5.2	6.4	6.9	7.1	10.2	5.8
	0.20–0.35	38.6	40.1	45.7	49.0	56.0	56.9	57.8	48.2
	0.40–0.55	41.1	38.5	37.0	34.9	31.5	30.9	26.9	35.1
	0.60–0.75	13.3	13.4	10.3	8.4	5.0	4.7	4.4	9.0
	0.80–0.95	2.7	3.8	1.5	1.2	0.7	0.4	0.4	1.6
	1.00–1.15	0.6	0.6	0.3	0.1	...	...	0.4	0.3
	1.20–1.35	0.2	...	...	...	...	...	...	

been noted by other authors,[7,8] who noted the same trends as described here. Precise comparisons of our statistics to theirs would be difficult and not altogether meaningful because of the marked difference of technic and method of approach to the problem. All previous series have utilized separate R and S wave amplitude determinations rather than a combined measurement for maximum QRS amplitude, and no series, to our knowledge, has separated final statistics into five-year segments of the adult population.

T Wave Amplitude: T wave amplitude was calculated in the four leads utilized during the QRS amplitude study, namely I, aVF, V_2 and V_6. The amplitude was measured using the T-P interval as the baseline. If the T wave was biphasic, the distance from the highest to the lowest point was measured. Table XXXVII provides the percentage distribution by age group for the T wave amplitude in the four individual leads and Table XXXVIII provides the quartiles. Figure 9 illustrates this same information in terms of cumulative per cent. In this figure, as with those concerning QRS amplitudes, only the first, fourth and seventh age groups are illustrated for purposes of clarity. In each lead, the oldest, middle and youngest age groups appear from left to right showing the change of distribution of T wave amplitude between the age groups. The fact that the decrease of T wave amplitude in lead I with age was less marked than in the other leads is dependent upon the coincident leftward rotation of the T wave vector in the frontal plane (refer also to discussion of QRS amplitude in lead I).

Measurement of the total voltage of the forces of ventricular recovery was estimated using cal-

TABLE XXXVIII
T Wave Amplitude in Leads I, aVF, V_2 and V_6
Quartiles by Age Group*

Lead	Quartile	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I	First	0.25	0.25	0.25	0.25	0.20	0.20	0.20	0.20
	Second	0.30	0.30	0.30	0.30	0.25	0.25	0.25	0.30
	Third	0.35	0.35	0.35	0.35	0.35	0.30	0.30	0.35
aVF	First	0.25	0.20	0.20	0.15	0.15	0.15	0.15	0.15
	Second	0.30	0.25	0.25	0.20	0.20	0.20	0.20	0.25
	Third	0.40	0.35	0.30	0.30	0.30	0.25	0.25	0.35
V_2	First	0.55	0.55	0.50	0.50	0.45	0.45	0.45	0.50
	Second	0.70	0.70	0.65	0.60	0.60	0.60	0.60	0.65
	Third	0.90	0.85	0.80	0.80	0.75	0.75	0.75	0.85
V_6	First	0.30	0.30	0.30	0.25	0.25	0.25	0.25	0.25
	Second	0.40	0.40	0.35	0.35	0.30	0.30	0.30	0.35
	Third	0.50	0.50	0.45	0.40	0.40	0.40	0.40	0.50

* All figures shown are in millivolts.

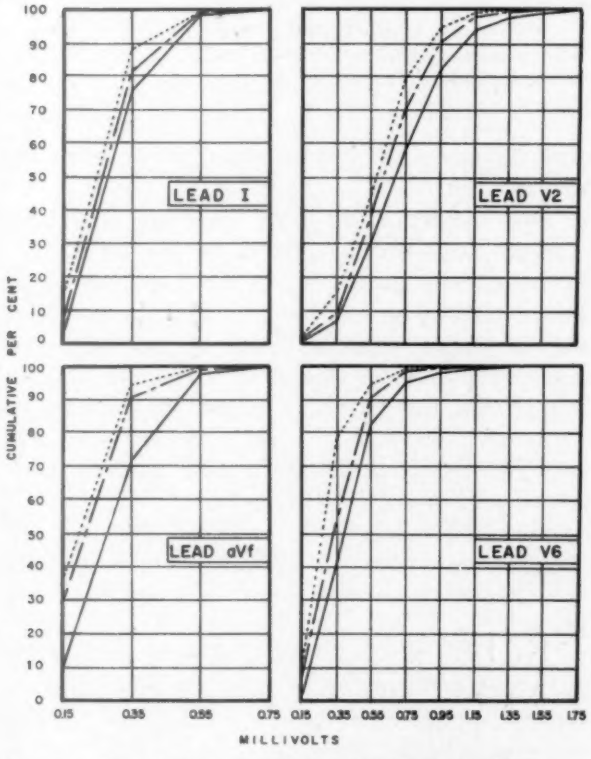


FIG. 9. Cumulative percentage distributions of T wave amplitude for the sixteen- to nineteen-year group (solid line), thirty- to thirty-four-year group (dash-dot line), and forty-five years and over group (broken line). In each lead there is some decrease of the distribution of measurable voltage with successively older age groups.

culations similar to those utilized in the QRS amplitude study, namely leads I + aVF, V_2 + V_6 and I + aVF + V_2. Table XXXIX gives the percentage distribution by age group for these values and Table XL provides the quartiles. Figure 10 gives a graphic representation of the information contained in Table XXXIX with the individual percentages converted to cumulative percentages. Inspection of these figures and of the tables reveals that the total T amplitude decreases with age regardless of whether it is measured in the frontal or transverse planes or spatially. That T wave amplitude decreases with age in both the frontal (leads I + aVF) and in the transverse (leads V_2 + V_6) planes indicates that an observed decrease of T wave amplitude in any individual lead may not be solely attributed to rotation of the T vector. The decrease in the sum of the T wave amplitude in leads I, aVF and V_2 with age further demonstrates the change noted in older age groups than can be evaluated by spatial measurements.

SUMMARY

A detailed analysis has been carried out on 6,014 normal electrocardiograms obtained from asymptomatic healthy men examined for flying status with the U. S. Air Force. These records were selected by a random process, approx-

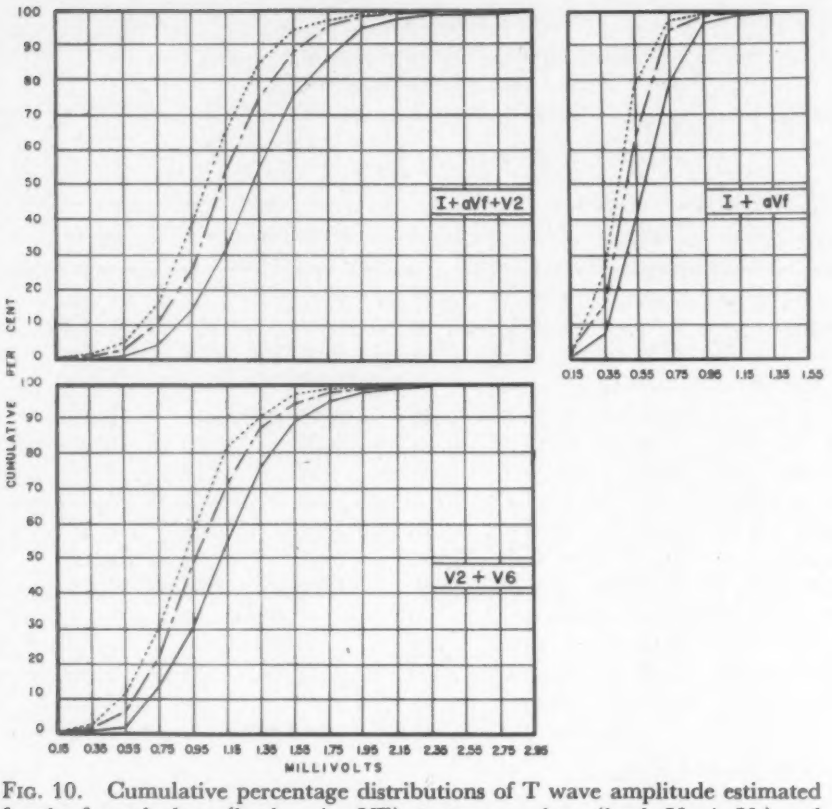


FIG. 10. Cumulative percentage distributions of T wave amplitude estimated for the frontal plane (leads I + aVF), transverse plane (leads $V_2 + V_6$) and spatially (leads I + aVF + V_2). Solid line, sixteen- to nineteen-year group; dash-dot line, thirty- to thirty-four-year group; broken line, forty-five years and over group. These curves illustrate that the total measurable voltage of ventricular recovery also decreases with each older age group.

imately 1,000 for each five-year age group of the adult age range represented by Air Force personnel. The rigid physical requirements to which these men are subjected provide a survey population which has an incidence of cardiac disease as low as any segment of the American population.

The age of the subjects ranged from sixteen through fifty-eight years. The height of the subjects ranged from 62 to 77 inches and there was no apparent variation with age. The weight of the subjects varied from 100 to 269 pounds. The older age groups showed a marked increase of weight for height (relative weight).

The heart rate varied from 39 to 129 beats per minute with some slight increase of rate in the older age groups.

P wave duration ranged from 0.06 through 0.15 second, with a median of 0.11 second. The range of P wave amplitude was from 0.05 through 0.35 mv. P axis in the frontal plane ranged from −30 through +90 degrees with 95 per cent of records falling between +15 and +75 degrees. There was no apparent variation between age groups for any of these determinations.

The range of the P-R interval was 0.10 through 0.20 second, although the latter was arbitrarily set as the upper limit of normal at the beginning of the study. The median was 0.16 second. The incidence of P-R intervals greater than 0.20 second in the same subject population was given in a previous article in this series and found to be extremely low. It was concluded that 0.20 second may be considered the upper limit of normal.

The Q-T interval varied from 0.24 through 0.47 second with a median of 0.38 second. There was little variation between the age groups.

The Q-U interval varied from 0.40 through 0.71 second with a median of 0.56 second. There appeared to be some increase in this value in the older age groups.

The QRS duration ranged from 0.05 to 0.11 second with a median and mode at 0.08 second. The incidence of QRS durations above 0.10 second was low.

The duration of the R wave in lead V_2 ranged

TABLE XXXIX

T Wave Amplitude Measured in the Frontal and Transverse Planes and Spatially
Percentage Distribution by Age Group

Combinations of Amplitudes from Indicated Coordinate Leads	T Wave Amplitude (mv.)	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I + aVF (frontal plane)	0.00–0.15	0.2	...	0.2	1.3	0.6	0.4	0.7	0.4
	0.20–0.35	7.4	10.0	13.2	15.8	19.4	18.8	25.4	14.8
	0.40–0.55	34.6	40.1	45.8	47.0	51.8	55.0	52.5	45.8
	0.60–0.75	37.4	37.3	32.2	30.2	24.1	22.7	19.0	30.0
	0.80–0.95	17.6	11.2	7.9	5.3	3.9	2.7	2.0	8.0
	1.00–1.15	2.5	1.3	0.6	0.2	0.2	0.4	0.4	0.9
	1.20 and over	0.2	0.2	...	0.1	...	...	...	0.1
$V_2 + V_6$ (transverse plane)	0.00–0.15	...	...	...	...	...	0.1	...	0.7
	0.20–0.35	0.1	0.1	0.9	0.7	1.3	0.6	1.5	
	0.40–0.55	2.0	2.1	3.5	5.7	7.1	5.8	10.8	4.8
	0.60–0.75	11.3	11.6	13.9	16.0	19.4	18.8	18.8	15.3
	0.80–0.95	17.3	19.8	22.5	26.9	25.0	29.2	27.1	23.4
	1.00–1.15	25.5	25.0	25.7	22.2	24.4	23.9	24.1	24.5
	1.20–1.35	20.1	19.1	15.6	15.6	13.7	13.5	10.4	15.9
	1.40–1.55	12.3	11.8	11.1	7.5	6.0	5.2	4.9	8.8
	1.60–1.75	5.8	6.0	4.0	3.4	2.1	1.9	1.3	3.7
	1.80–1.95	3.7	2.8	1.8	1.3	0.7	1.0	0.7	1.9
	2.00–2.15	1.1	1.3	0.8	0.5	0.3	...	0.2	0.6
	2.20–2.35	0.6	0.2	0.3	0.1	...	...	0.2	0.2
I + aVF + V_2 (spatially)	0.20–0.35	...	...	...	0.2	0.6	0.2	0.4	0.2
	0.40–0.55	0.5	0.4	1.3	2.1	2.2	2.2	3.8	1.6
	0.60–0.75	3.4	3.3	6.8	8.0	11.1	9.3	13.2	7.4
	0.80–0.95	9.9	15.7	15.7	16.6	20.4	22.2	21.2	16.9
	1.00–1.15	17.9	17.8	23.3	27.2	24.1	25.0	26.7	22.7
	1.20–1.35	22.9	24.9	20.4	20.7	21.6	23.5	19.0	22.1
	1.40–1.55	21.6	18.8	16.1	13.9	12.8	10.8	9.9	15.4
	1.60–1.75	10.3	10.1	8.7	7.0	4.5	4.3	3.7	7.3
	1.80–1.95	8.3	4.7	5.4	2.9	2.0	1.7	1.5	4.1
	2.00–2.15	3.1	2.9	1.4	1.0	0.6	0.5	0.2	1.5
	2.20–2.35	1.7	0.9	0.5	0.2	0.1	0.1	0.4	0.6
	2.40–2.55	0.3	0.3	0.2	0.0	...	...	0.0	0.1
	2.60–2.75	0.0	0.1	0.1	0.1	...	...	0.2	0.1

from zero through 0.06 second with a median at 0.03 second, and the duration of the S wave in lead V_2 varied from 0.01 through 0.08 second with a median at 0.05 second.

The QRS axis in the frontal plane ranged from −90 through +120 degrees with few subjects at both extremes. There was a shift to the left of the QRS axis with each older age group independent of QRS amplitude and body weight changes. QRS transitions were found at all six precordial leads with the majority (91.6 per cent) in leads V_2 through V_4. There was little variation between age groups in the distribution of QRS transitions.

The T axis in the frontal plane ranged from −15 through +90 degrees with few subjects at both extremes. The mode was +45 degrees and there appeared to be some leftward rotation of the T vector in the frontal plane in the older age groups. The T transition in the transverse plane was almost invariably near lead V_1.

The mean spatial QRS-T angle ranged between zero and +139 degrees with 96 per cent of the series falling below +70 degrees. Our data did not support a previous concept that the upper limit of normal for the QRS-T angle is 50 degrees; 18 per cent of records in our series were of this or a greater angle.

An S-T segment vector in the frontal plane as evidenced by S-T segment elevation was noted

TABLE XL

T Wave Amplitude Measured in the Frontal and Transverse Planes and Spatially Quartiles by Age Group*

Combinations of Amplitudes from Indicated Coordinate Leads	Quartile	Age Group (yr.)							
		<20	20–24	25–29	30–34	35–39	40–44	45 and >	All
I + aVF (frontal plane)	First	0.50	0.47	0.45	0.43	0.41	0.42	0.39	0.44
	Second	0.64	0.59	0.55	0.53	0.51	0.51	0.49	0.55
	Third	0.77	0.73	0.69	0.67	0.62	0.60	0.58	0.69
$V_2 + V_6$ (transverse plane)	First	0.93	0.91	0.86	0.81	0.77	0.79	0.73	0.83
	Second	1.15	1.13	1.07	1.00	0.97	0.96	0.93	1.04
	Third	1.38	1.37	1.31	1.24	1.18	1.17	1.13	1.27
I + aVF + V_2 (spatially)	First	1.12	1.06	1.01	0.97	0.90	0.91	0.87	0.98
	Second	1.35	1.30	1.22	1.17	1.13	1.12	1.08	1.21
	Third	1.58	1.53	1.49	1.40	1.35	1.33	1.30	1.45

* All figures shown are in millivolts.

in approximately 25 per cent of the series. There was a slight decrease in the incidence of detectable S-T segment elevation in the older age groups. The vector for S-T interval was, for the most part, between +60 and +90 degrees, and the greatest amplitude of S-T segment elevation ranged between 0.05 and +0.25 mv. with the majority in the range of 0.05 through 0.10 mv.

An estimation of the presence or absence of S-T segment elevation in the precordial leads and the direction of the S-T vector when present was made. Only 8.8 per cent of the entire series had no S-T segment elevation in any precordial lead. The greatest amplitude in any precordial lead ranged between 0.1 and 0.5 mv. with a general reduction in the incidence of the higher amplitudes in the older age groups.

The presence or absence, duration and amplitude of Q waves in leads I, II, III, aVL and aVF were determined. There were very few records with Q waves of 0.04 second duration and all of these were found in lead III. Q waves of lesser duration were common. Q waves in leads I and aVL were not as frequent as those in leads II, III and aVF, but were found in association with vertical and horizontal QRS axes about equally; Q waves in leads II, III and aVF were very rarely associated with horizontal QRS axes.

The P-R interval minus P wave duration value was calculated for all records; approximately 10 per cent of subjects had an isoelectric P-R segment of 0.03 second or less.

QRS amplitude was determined by vector methods, not as analysis of individual leads and individual R or S waves. The correlation coefficients for QRS amplitude, age, QRS axis and body weight were computed. It was found that measurable QRS amplitude whether considered in the frontal or transverse planes or spatially tends to decrease from the younger to the older age groups regardless of the effect of QRS axis or body weight changes. Body weight and QRS amplitude were not related. It is proposed that serial electrocardiograms may become a means of assessing the aging process of the heart.

T wave amplitude was analyzed similarly to QRS amplitude and was found to decrease in the older age groups.

The incidence of a terminal QRS vector creating an S_1S_2 and an $S_1S_2S_3$ pattern was determined; 15 per cent of all records showed the former and 24 per cent showed the latter. These patterns represent minor normal variations of intraventricular conduction.

The ratio of the amplitude of the R to the S wave in leads V_1 and V_2 was determined and found greater than 1 in 0.7 per cent, and 8.5 per cent of records, respectively.

ACKNOWLEDGMENT

We are deeply indebted to Mrs. Katherine Gregg, Mr. Robert Dedeke and Mrs. Dorothy Ball of the Biometrics Branch at the School of Aviation Medicine for their extensive contribution to this paper with the

IBM processing and statistical presentation. We also wish to extend our sincere thanks for the painstaking efforts of the following technicians: SSgt. Charles Adams, SSgt. Merle Thomas, A/1c Ralph Jackson, A/3c Loren Askelson and A/1c Harvey Hamel.

References

1. Stewart, C. B. and Manning, G. W. A detailed analysis of 500 RCAF aircrew. *Am. Heart J.*, 27: 502, 1944.
2. Graybiel, A., McFarland, R. A., Gates, D. C. and Webster, F. A. Analysis of the electrocardiograms obtained from 1000 young healthy aviators. *Am. Heart J.*, 27: 524, 1944.
3. Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart, 5th ed., p. 135. New York, 1953. New York Heart Association.
4. Simonson, E. Principles for determination of electrocardiographic normal standards. *Am. Heart J.*, 52: 163, 1956.
5. Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. I. Incidence of abnormalities. *Am. J. Cardiol.*, 6: 76, 1960.
6. Air Force Manual 160-1, Medical Examination, April 30, 1953, p. 96.
7. Packard, J. M., Graettinger, J. S. and Graybiel, A. Analysis of the electrocardiograms obtained from 1,000 young healthy aviators. Ten-year follow-up. *Circulation*, 10: 384, 1954.
8. Simonson, E. and Keys, A. The effect of age and body weight on the electrocardiograms of healthy men. *Circulation*, 6: 749, 1952.
9. Ashman, R. and Hull, E. Essentials of Electrocardiography, 2nd ed. New York, 1941. The Macmillan Co.
10. White, P. D., Leach, C. E. and Foote, S. A. Errors in measurement of PR (PQ) interval and QRS duration in the electrocardiogram. *Am. Heart J.*, 22: 321, 1941.
11. Kossmann, C. E. The normal electrocardiogram. *Circulation*, 8: 920, 1953.
12. Johnson, R. L., Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. VII. Atrioventricular block. *Am. J. Cardiol.*, 6: 153, 1960.
13. White, N. S., Kossmann, C. E. and Ershler, I. The effect of high altitude and of rebreathing on the duration of electrical systole in man. *Am. Heart J.*, 24: 230, 1942.
14. Lepeschkin, E. and Surawicz, B. The duration of the QU interval and its components in electrocardiograms of normal persons. *Am. Heart J.*, 46: 9, 1953.
15. Sokolow, N. and Friedlander, R. D. The normal unipolar precordial and limb lead electrocardiogram. *Am. Heart J.*, 38: 665, 1949.
16. Lamb, L. E. Fundamentals of Electrocardiography and Vectorcardiography, p. 64. Springfield, Ill., 1957. Charles C Thomas.
17. Grant, R. P. and Estes, E. H., Jr. Spatial Vector Electrocardiography. Philadelphia, 1951. The Blakiston Co.
18. Smith, G. B., Jr., Averill, K. H. and Lamb, L. E. Electrocardiographic findings in 67,375 asymptomatic subjects. IX. Myocardial infarction. *Am. J. Cardiol.*, 6: 190, 1960.

This Symposium on Cardiology in Aviation was conducted at The School of Aviation Medicine, USAF Aerospace Medical Center (ATC), Brooks Air Force Base, San Antonio, Texas, on November 12 and 13, 1959. It was sponsored by the Aerospace Medical Association, Air Line Medical Directors Association and the School of Aviation Medicine.

after a myocardial infarction
and throughout the course
of postcoronary convalescence...

Peritrate helps establish and sustain collateral circulation

1. improves coronary blood flow with no significant drop in blood pressure or increase in pulse rate
2. helps support natural healing and repair
3. helps reduce myocardial damage
4. smooth onset of action minimizes nitrate headache

basic therapy in coronary artery disease

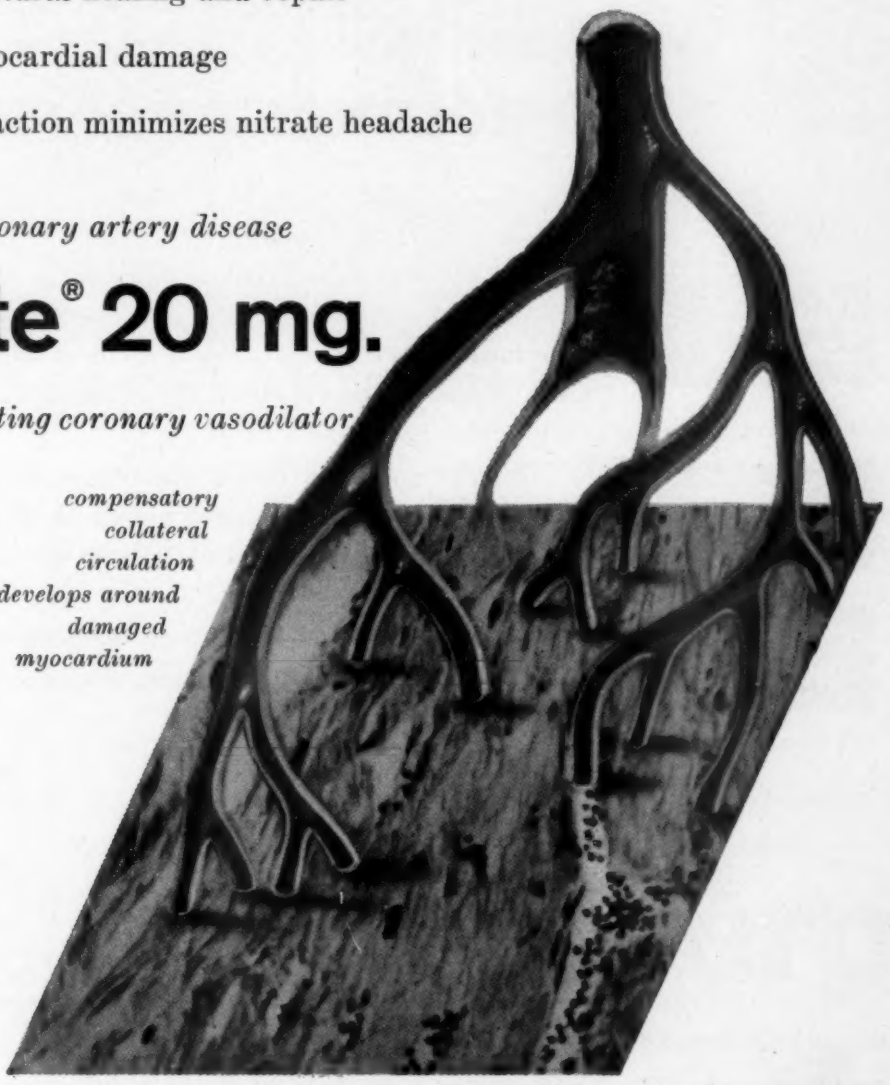
Peritrate® 20 mg.

brand of pentaerythritol tetranitrate

the selective, long-acting coronary vasodilator

WARNER
CHILCOTT
MORRIS PLAINS, N.J.

GP-02



compensatory collateral circulation develops around damaged myocardium

FOR ANGINA

Nitroglycerin is the drug of choice for the **ACUTE ATTACK**

'CARDILATE'

may well be chosen for **PROLONGED PROPHYLAXIS**

CLINICAL OPINION

"... the magnitude of the response to 15 mg. ['Cardilate'] was comparable to that following nitroglycerin.... The comparatively prolonged duration of action of erythrol tetranitrate when given sublingually makes it especially valuable for clinical use."[1]

CLINICAL OPINION

"Nitroglycerin and erythrol tetranitrate when administered sublingually are among the most potent of all prophylactic agents available for the treatment of patients with angina pectoris."[2]

CLINICAL OPINION

"Erythrol tetranitrate exhibits an inherent long-acting vasodilating effect. Therefore it is the drug of choice in angina pectoris."[3]

'CARDILATE' brand
Erythrol Tetranitrate Sublingual Tablets

NEW

5 mg., scored 

15 mg., scored 

Bottles of 100 tablets.

Complete literature available on request.

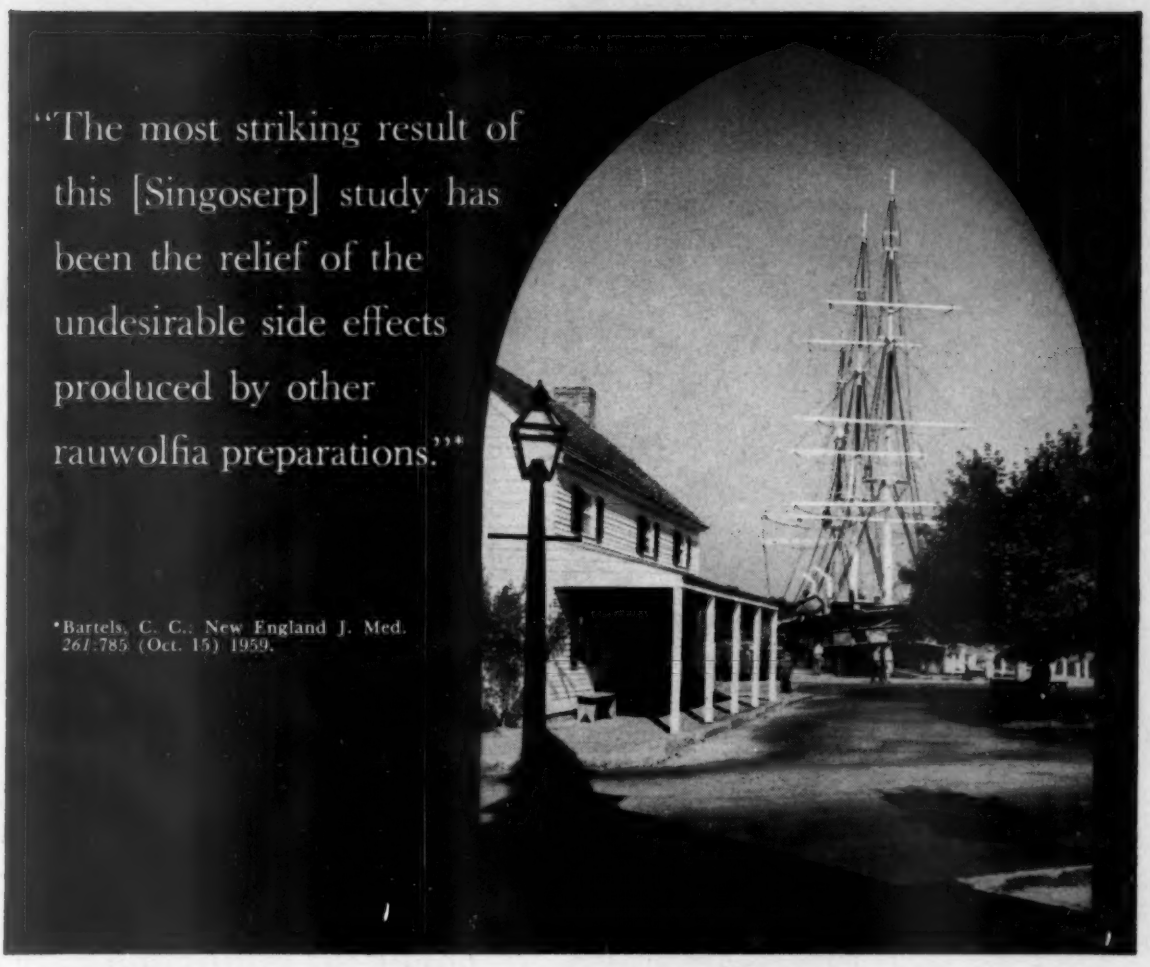
1. Riseman, J.E.F., *et al.*: Circulation *17*:22 (Jan.) 1958.

2. Russek, H.I.: Circulation *18*:774 (Oct.) 1958.

3. Hirshleifer, I., *et al.*: Scientific Exhibit, A.M.A., Atlantic City, N. J., June, 1959.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

from the New England Journal of Medicine:



results you can confirm in your practice:

"In 24 cases syrosingopine was substituted for the rauwolfia product because of 26 troublesome side effects; these symptoms were relieved in all but 3 patients."*

Side Effects	Incidence with Prior Rauwolfia Agent	Incidence with Singoserp
Depression	11	1
Lethargy or fatigue	5	0
Nasal congestion	7	0
Gastrointestinal disturbances	2	2
Conjunctivitis	1	0

(Adapted from Bartels*)

many hypertensive patients prefer

Singoserp®

(syrosingopine CIBA)

because it lowers their blood pressure without rauwolfia side effects

Tablets, 1 mg. (white, scored); bottles of 100.

CIBA
SUMMIT, NEW JERSEY

Complete information available on request.

8/2779MB

COUMADIN BIBLIOGRAPHY

Published studies on anticoagulant therapy with COUMADIN

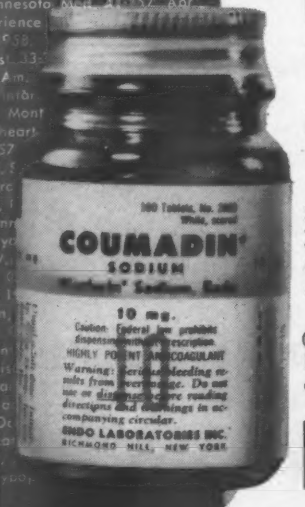
1. Friedman, B.: The use of anticoagulants in the treatment of coronary and cerebral vascular disease, J. Tennessee M. A. 52:171, May, 1959. 2. Shapiro, S.: Long term therapy of coronary arteriosclerosis, Angiology 10:126, Apr., 1959. 3. Vastola, E. F., and Frugh, A.: Anticoagulants for occlusive cerebrovascular lesions, Neurology 9:143, Mar., 1959. 4. Toohey, M.: Clinical experience with warfarin sodium, Brit. M. J. 2:892, Oct. 11, 1958. 5. Forter, R. R.; Richardson, D., and Mauck, H. P., Jr.: Clinical experiences with the anticoagulant warfarin sodium ("Coumadin Sodium"), Virginia M. Month. 85:465, Sept., 1958. 6. Trumble, E. A.: Clinical experience with intramuscular warfarin sodium (Coumadin Sodium), Surg. Gynec. & Obst. 107:303, Sept., 1958. 7. Goodman, D. H.: Early clue to visceral carcinoma—hemorrhage after intravenously given warfarin, J.A.M.A. 166:1037, Mar. 1, 1958. 8. Shapiro, C. M.; Lisker, R.; Lichtman, A. M., and Josephson, A. M.: Comparative clinical study of Coumadin Sodium and Dicumarol in patients with thromboembolic diseases, Am. Heart J. 55:66, Jan., 1958. 9. Yarrow, M. W., Baer, S.; Kravitz, C., and Markson, V.: A preliminary report on sodium warfarin (Coumadin), J. Albert Einstein M. Center 5:205, June, 1957. 10. Baer, S.; Yarrow, M. W.; Kravitz, C., and Markson, V.: Clinical experiences with warfarin (Coumadin) sodium as an anticoagulant, J.A.M.A. 167:704, June 7, 1958. 11. Fremont, R. E., and Jagendorf, B.: Clinical observations on use of warfarin (Coumadin) sodium, a new anticoagulant, J.A.M.A. 165:1381, Nov. 16, 1957. 12. Shapiro, S., and Ciferri, F. E.: Intramuscular administration of the anticoagulant warfarin (Coumadin) sodium, J.A.M.A. 165:1377, Nov. 16, 1957. 13. Nicholson, J. H.: Clinical experiences with anticoagulants: A comparison of Coumadin (warfarin) Sodium and Dicumarol (bishydroxycoumarin), Angiology 8:456, O t., 1957. 14. Kerrin, H. F.; Guidot, J., and Wilhelm, S. K.: Clinical experiences with the anticoagulant Coumadin (warfarin) Sodium, Angiology 8:302, June, 1957. 15. Goodman, D. H.: Experience with a new anticoagulant Coumadin® (warfarin) Sodium, Arizona Med. 13:389, Oct., 1956. 16. Nicholson, J. H., and Leavitt, T., Jr.: Coumadin (warfarin) Sodium: A new anticoagulant, New England J. Med. 255:491, Sept. 13, 1956. 17. Clatanoff, D. V., and Meyer, O. O.: Further observations on use of warfarin sodium in anticoagulant therapy, A.M.A. Arch. Int. Med. 97:753, June, 1956. 18. Freeman, D. J., and Meyer, O. O.: Rectal administration of warfarin (Coumadin) sodium. Sodium [3 (2-acetonyl-benzyl)-4 hydroxycoumarin], Proc. Soc. Exper. Biol. & Med. 92:52, May, 1956. 19. Pollock, B. E.: Clinical experience with Coumadin Sodium, a new anticoagulant drug, Angiology 6:506, Dec., 1955. 20. Pollock, B. E.: Clinical experience with warfarin (Coumadin) sodium, a new anticoagulant, J.A.M.A. 159:1094, Nov. 12, 1955. 21. Shapiro, S.: The hypoprothrombinemia-inducing activity of warfarin sodium (Coumadin® Sodium), J. Kansas M. Soc. 55:687, Dec. 1954. 22. Clatanoff, D. V.; Triggs, P. O., and Meyer, O. O.: Clinical experience with coumarin anticoagulants warfarin and warfarin sodium, A.M.A. Arch. Int. Med. 94:213, Aug. 1954. 23. Shapiro, S.: Warfarin sodium derivative (Coumadin® Sodium): An intravenous hypoprothrombinemia-inducing agent, Angiology 4:380, Aug., 1953.

Other published literature referring to Endo's COUMADIN

24. Escudero, J.; McDevitt, E., and Wright, I. S.: Dicumarol, Coumadin, Marcumar and Tromexan: Comparative study of their action on the clot as registered by the thrombelastogram, Circulation 20:403, Sept., 1959. 25. Hillier, W. F., Jr.: Little strokes, West Virginia M. J. 55:259, Aug. 1959. 26. Wright, I. S.: Strokes; the present status of diagnosis and treatment, Postgrad. Med. 25:549, May, 1959. 27. Little, J. R.: Purpura fulminans treated successfully with anticoagulation, J.A.M.A. 169:104, Jan. 3, 1959. 28. Link, K. P.: The discovery of Dicumarol and its sequels, Circulation 19:97, Jan., 1959. 29. Kleiner, I. S., and Orten, J. M.: Human Biochemistry, ed. 5, Mosby, St. Louis, 1958, pp. 211-212. 30. Meyer, O. O.: Use of anticoagulan[illegible] in the treatment of coronary artery disease, Postgrad. Med. 24:110, Aug., 1958. 31. Toohey, M.: Long-term anticoagulant therapy for coronary thrombosis, Brit. M. J. 2:473, Aug. 23, 1958. 32. McDevitt, E.; Wright, I. S., and Foley, W. T.: Present status of anticoagulant treatment of cerebral vascular lesions, M. Clin. North America, May, 1958, p. 587. 33. Barker, N. W.: Fundamentals of anticoagulant therapy, Minnesota Med. 41:352, Apr., 1958. 34. Grant, W. G., and MacMillan, R. L.: Experience [illegible] coagulant therapy, Canad. M. A. J. 78:317, Mar., 1958. [illegible] Treatment of peripheral arterial disease, Dis. Ches[illegible] 33:[illegible] Bratman, I.: Anticoagulants in myocardial infarction, Am. [illegible] 1958. 37. Toohey, M.: Anticoagulants in myocardial infar[illegible] Feb. 1, 1958. 38. Editorial: Warfarin, Virginia M. Mont[illegible] 39. Friedberg, C. K.: Recent advances in coronary heart[illegible] agement, New York J. Med. 57:3643, Nov. 15, 1957. [illegible] sodium as a long-term anticoagulant, M. Science 7[illegible] J. H., and Oglesby, P.: Long-term anticoagulant therc[illegible] 105:61, July, 1957. 42. Ware, A. G., and Strag[illegible] Elimination of some commonly occurring pitfalls, Ann[illegible] 1957. 43. Briner, D. H.: A study of 235 cases o[illegible] myo[illegible] Osteopath. A. 56:349, Feb., 1957. 44. Cosgriff, [illegible] W., coronary artery disease, Am. J. Chron. Dis. 4:402, [illegible] S. A., and Aird, R. B.: M. Clin. North America, Sept., 1[illegible] B. E.: The early management of myocardial infarction, [illegible] 1956. 47. Shapiro, S.: Anticoagulant therapy, Surg. [illegible] 1956, p. 469. 48. Wright, I. S.: Present status of an[illegible] treatment of myocardial infarction; the use and mis[illegible] evaluation of new anticoagulants, their indications a[illegible] 43:942, Nov., 1955. 49. Shapiro, S. (editorial): The a[illegible] prothrombinemia-inducing drugs, Angiology 6:498, Oc[illegible] Principles of anticoagulant therapy and their applica[illegible] ica, Jan., 1955, p. 227. 51. Shapiro, S., and Sp[illegible] (ascorbic acid plus "P" factors) in drug-induced [illegible] ology 5:64, Apr. 1954.

Coumadin is the original and only warfarin sodium responsible for establishing this drug as "the best anticoagulant available today"[30]

(over 50 published papers since 1953)



COUMADIN®

FOR ORAL, INTRAVENOUS OR INTRAMUSCULAR USE

SODIUM

IN MYOCARDIAL INFARCTION AND OTHER THROMBOEMBOLIC DISORDERS

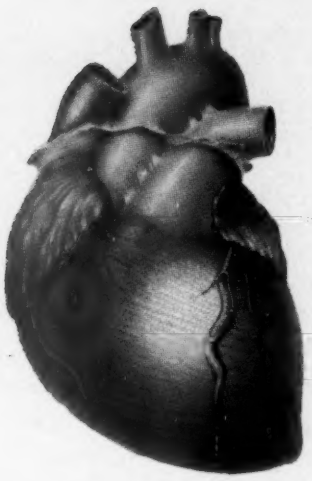
SUPPLIED: ***Oral***—scored tablets, 2 mg., 5 mg., 7½ mg., 10 mg., 25 mg. ***Parenteral***—single injection units, consisting of one vial, 75 mg., and one 3-cc. ampul Water for Injection.

COUMADIN (warfarin) Sodium is manufactured under license from the Wisconsin Alumni Research Foundation... *clinically established by Endo.*

Complete Information and Reprints on Request

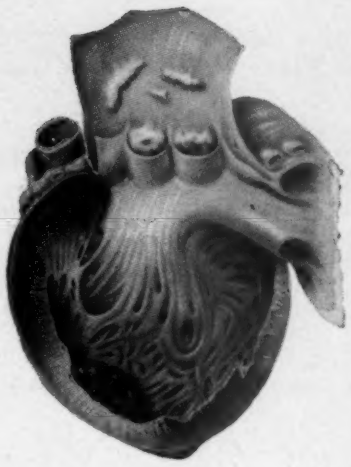
ENDO LABORATORIES
Richmond Hill 18, New York

Over 60,000,000 doses of Coumadin administered to date



IN ANGINA PECTORIS AND CORONARY INSUFFICIENCY

... the treatment must go further than vasodilation alone. It should also control the patient's ever-present anxiety about his condition, since anxiety itself may bring on further attacks.



AFTER MYOCARDIAL INFARCTION

... it is frequently not enough to boost blood flow through arterial offshoots and establish new circulation. The disabling fear and anxiety that invariably accompany the condition must be reduced, or the patient may become a chronic invalid.

Protects your coronary patient better than vasodilation alone

Unless the coronary patient's ever-present anxiety about his condition can be controlled, it can easily induce an anginal attack or, in cases of myocardial infarction, considerably delay recovery.

This is why Miltrate gives better protection for the heart than vasodilation alone in coronary insufficiency, angina pectoris and postmyocardial infarction. Miltrate contains not only PETN (pentaerythritol tetranitrate), acknowledged as basic therapy for long-acting vasodilation. What is more important – Miltrate provides Miltown, a tranquilizer of *proven* effectiveness in relieving anxieties, fear and day-to-day tension in over 600 clinical studies.

Thus, your patient's cardiac reserve is protected against his fear and concern about his condition...and his operative arteries are dilated to enhance myocardial blood supply.

Supplied: Bottles of 50 tablets. Each tablet contains 200 mg. Miltown and 10 mg. pentaerythritol tetranitrate.
Dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime, according to individual requirements.

REFERENCES

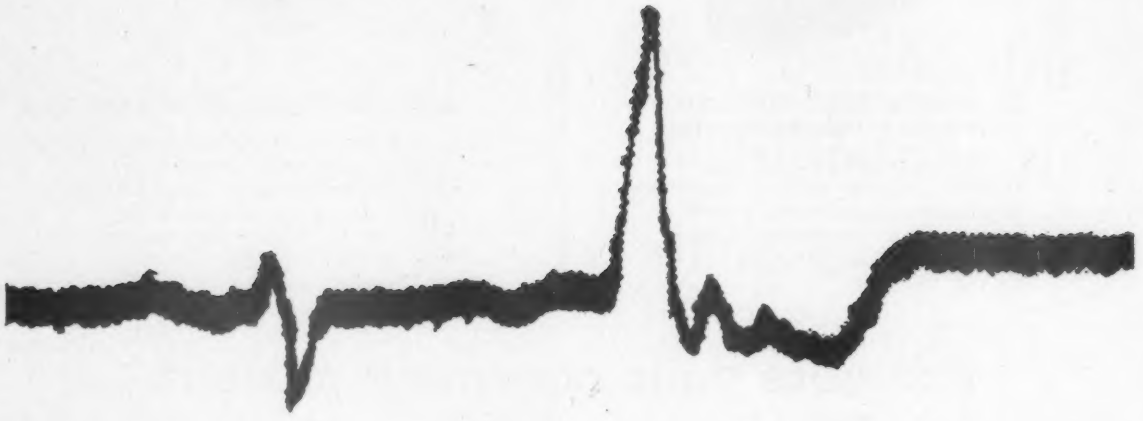
1. Ellis, L. B. *et al.:* Circulation *17*:945, May 1958. **2.** Friedlander, H. S.: Am. J. Cardiol. *1*:395, Mar. 1958. **3.** Riseman, J. E. F.: New England J. Med. *261*:1017, Nov. 12, 1959. **4.** Russek, H. I. *et al.:* Circulation *12*:169, Aug. 1955. **5.** Russek, H. I.: Am. J. Cardiol. *3*:547, April 1959. **6.** Tortora, A. R.: Delaware M. J. *30*:298, Oct. 1958. **7.** Waldman, S. and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075, July 1957.

Miltrate®

Miltown® (meprobamate) + PETN

WALLACE LABORATORIES / *New Brunswick, N.J.*

CWL-1388



for cardiac arrhythmias... obvious advantages

PRONESTYL® HYDROCHLORIDE

SQUIBB PROCAINE AMIDE HYDROCHLORIDE

Pronestyl offers obvious advantages over quinidine and procaine in the management of cardiac arrhythmias: "Procaine amide [Pronestyl] should be the drug of choice in arrhythmias of ventricular origin."[1]—on oral administration, side effects are less marked than with quinidine—administered I.V., Pronestyl is safer than a corresponding I.V. dose of quinidine—administered I.M., Pronestyl acts faster than I.M. quinidine[2]—Pronestyl sometimes stops arrhythmias which have not responded to quinidine[3,4]—Pronestyl may be used in patients sensitive to quinidine—more prolonged action, less toxicity, less hypotensive effect than procaine—no CNS stimulation such as procaine may produce.

Supply: For convenient oral administration: Capsules, 0.25 gm., in bottles of 100.
For I.M. and I.V. administration: Parenteral Solution, 100 mg. per cc., in vials of 10 cc.

References: 1. Zapata-Diaz, J., et al.: Am. Heart J. 43:854, 1952. 2. Modell, W.: In Drugs of Choice, C.V. Mosby Co., St. Louis, 1958, p. 454. 3. Kayden, H. J., et al.: Mod. Concepts Cardiovasc. Dis. 20:100. 1951. 4. Miller, H., et al.: J.A.M.A. 146:1004, 1951.

SQUIBB *Squibb Quality—the Priceless Ingredient*

in angina pectoris...

24-hour protection against both pain and fear with just one

COROVAS® Tymcap b.i.d.

Clinically proved[1,2,3] to establish peak nitrate blood levels soon after an initial dose and to maintain these levels throughout a 12-hour period...

thus avoiding bothersome t.i.d. or q.i.d. routines, yet permitting the patient to enjoy up to 12 hours' uninterrupted relief from pain and fear with a single COROVAS Tymcap: "...it would appear that 60 mg. of PETN in TD capsule form [timed-disintegration COROVAS Tymcaps] is as effective as 80 mg. PETN in tablet form, in controlling the anginal attacks."[3]

COROVAS Tymcaps

prolonged, sustained-action of vasodilating pentaerythritol tetranitrate (PETN) 30 mg., and sedative secobarbituric acid 50 mg.

- *controls or prevents anginal pain*
- *alleviates associated fear, apprehension and panic*
- *reduces frequency and severity of attacks*
- *reduces the need for nitroglycerin*

Supplied—Boxes of 60 and 120

1. Feinblatt, T. M., and Ferguson, E. A.: New Eng. J. Med. 256:331 (Feb.) 1957.
2. Kupersmith, I. H.: International Record of Medicine, Vol. 171 No. 10 (Oct.) 1958.
3. Berry, J. W., and Roach, T. C.: Circulation, Vol. 17, No. 6 (June) 1958.

Amfre-Grant Inc. Brooklyn 26, New York

Schering

in acute coronary occlusion

control in short- or long-term oral anticoagulant therapy Miradon®

anisindione

"excellent control . . . in 54 out of 59 cases [including 43 patients with coronary thrombosis]."[1]

rapid induction

"It leads to an initial rapid fall in prothrombin activity. . . ."[2] Therapeutic levels attained in 48 to 72 hours.

rapid recovery

"Normal prothrombin levels were recorded between 36 and 72 hours after cessation of treatment. . . ."[3]

prompt reversibility

Vitamin K_1 "... counteracted the effect of Miradon in a predictable fashion in 5 to 8 hours."[4]

prompt restoration

"The anticoagulant effect can be restored rapidly by remedication."[2]

stable maintenance

With MIRADON "... a very even response was evident during therapy."[3] "Once the prothrombin levels had been reduced to the therapeutic bracket, they were maintained there with little difficulty on daily doses of the drug."[5]

References: (1) Blaustein, A.: New York J. Med. *58*:701, 1958. (2) Lange, K., *et al.*: Am. Heart J. *55*:73, 1958. (3) Kellaway, G.: Brit. M. J. *2*:889, 1958. (4) Connell, W. F., and Mayer, G. A.: Canad. M.A.J. *80*:785, 1959. (5) Paul, H. A., Ascott, P. M., Koppel, J. L., and Olwin, J. H.: Surg. Gynec. & Obst. *108*:605, 1959.

5-640

REPRINT ORDER FORM

THE AMERICAN JOURNAL OF MEDICINE
11 E. 36th St., New York 16, N. Y.

Please send me the following reprints from THE AMERICAN JOURNAL OF MEDICINE.

☐ SYMPOSIUM ON RENAL PHYSIOLOGY $4.00

SEMINARS

☐ ALLERGY $2.00

☐ DISEASES OF THE PANCREAS $2.00

☐ BONE DISEASES $2.00

☐ LIVER DISEASE $2.00

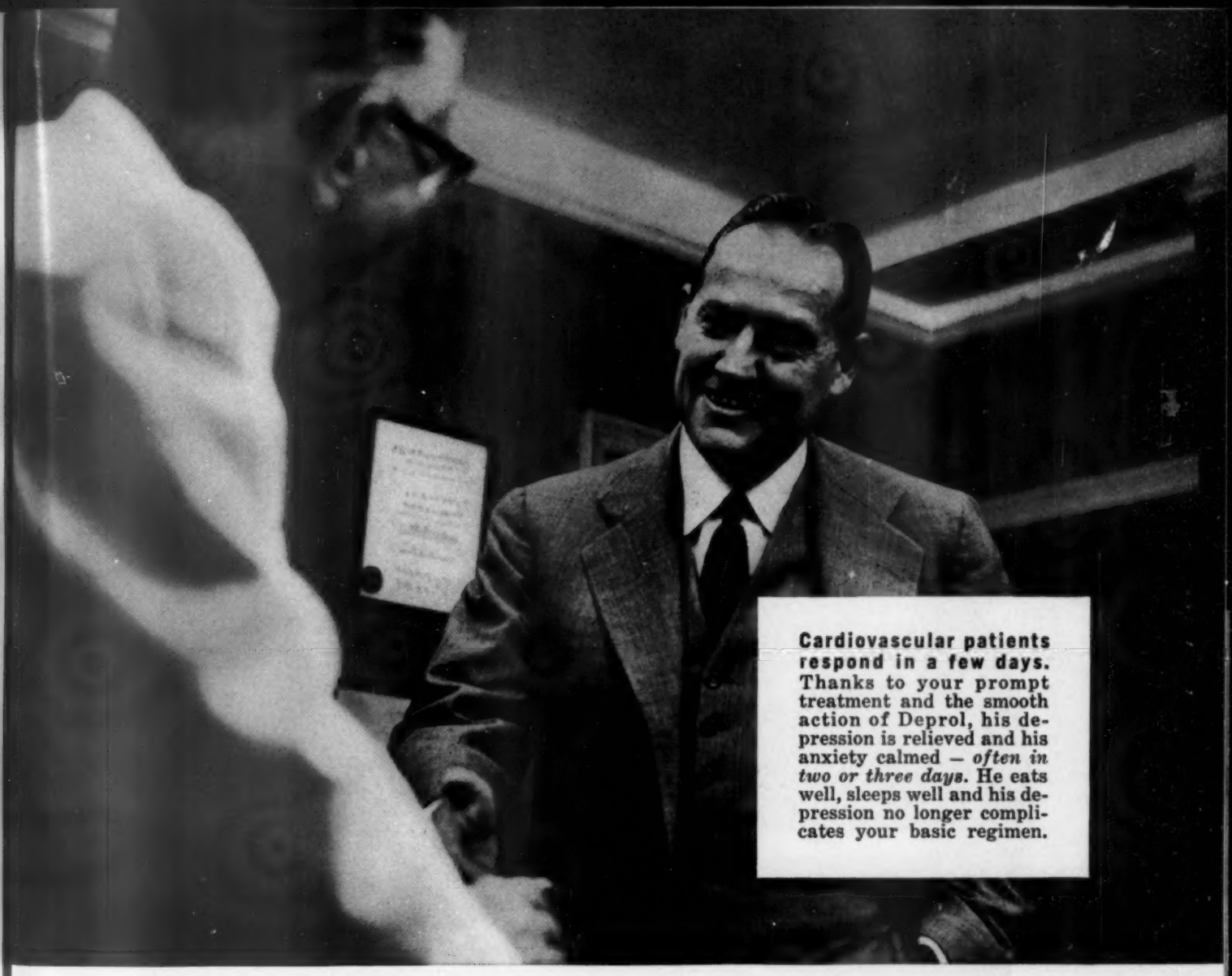
☐ MYCOTIC INFECTIONS $3.00

Enclosed is my check

Name_____

Address_____

City_____ State_____



Cardiovascular patients respond in a few days. Thanks to your prompt treatment and the smooth action of Deprol, his depression is relieved and his anxiety calmed – *often in two or three days.* He eats well, sleeps well and his depression no longer complicates your basic regimen.

Lifts depression...as it calms anxiety!

For cardiovascular patients–a smooth, balanced action that lifts depression as it calms anxiety...rapidly and safely

Balances the mood–no "seesaw" effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient – *they often aggravate anxiety and tension.* And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression.*

In contrast to such "seesaw" effects, Deprol lifts depression as it calms anxiety – both at the same time.

Acts swiftly–the patient often feels better, sleeps better, within two or three days. Unlike most other antidepressant drugs, Deprol relieves the patient quickly – often within two or three days.

Acts safely – no danger of hypotension. Deprol does not cause hypotension, tachycardia, jitteriness, or liver toxicity. It can be safely administered with basic cardiovascular therapy.

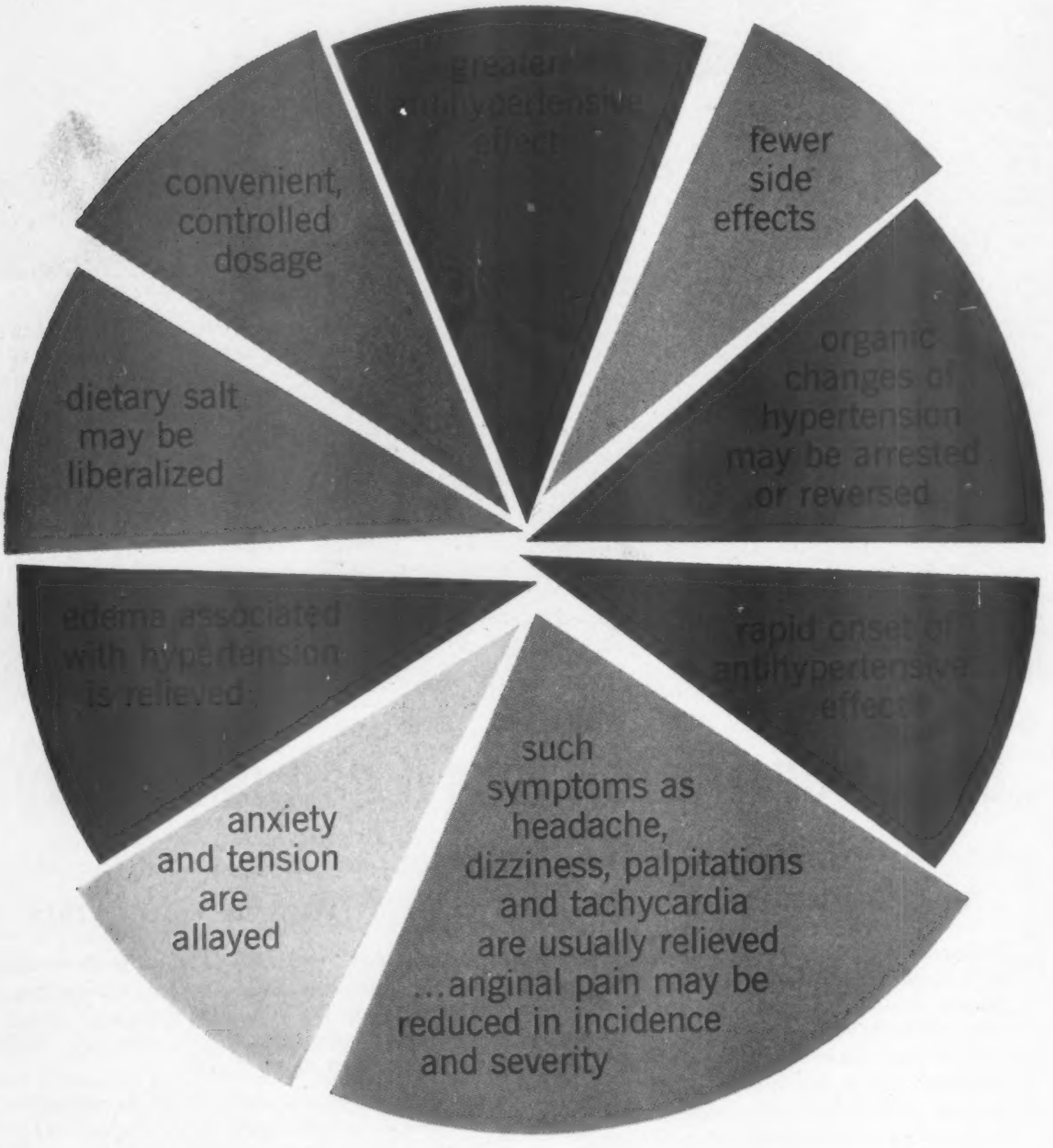
Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.
Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

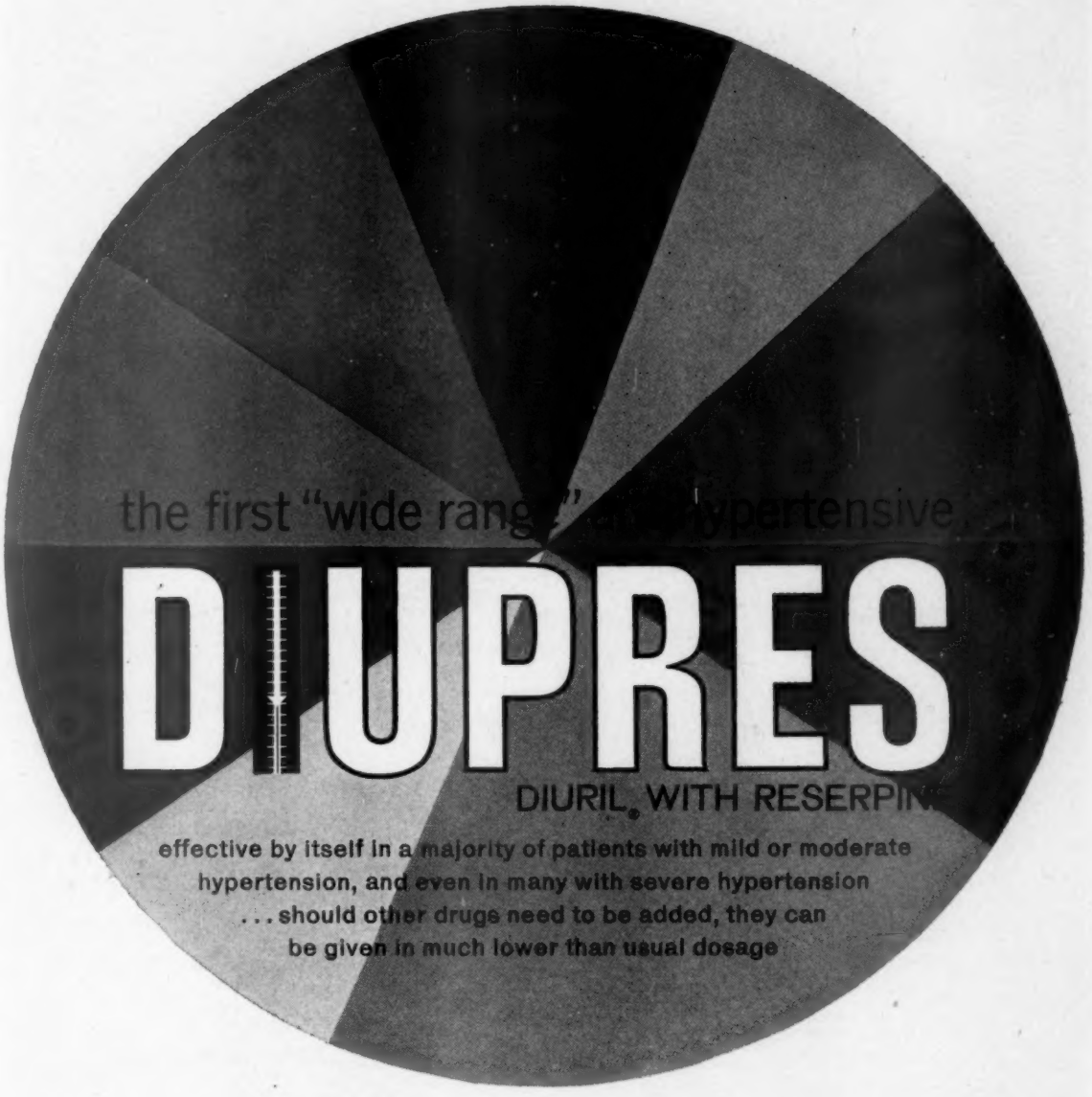
Deprol®

WALLACE LABORATORIES
New Brunswick, N. J.

CD-763

here are some of the ways hypertensive patients benefit when you prescribe DIUPRES





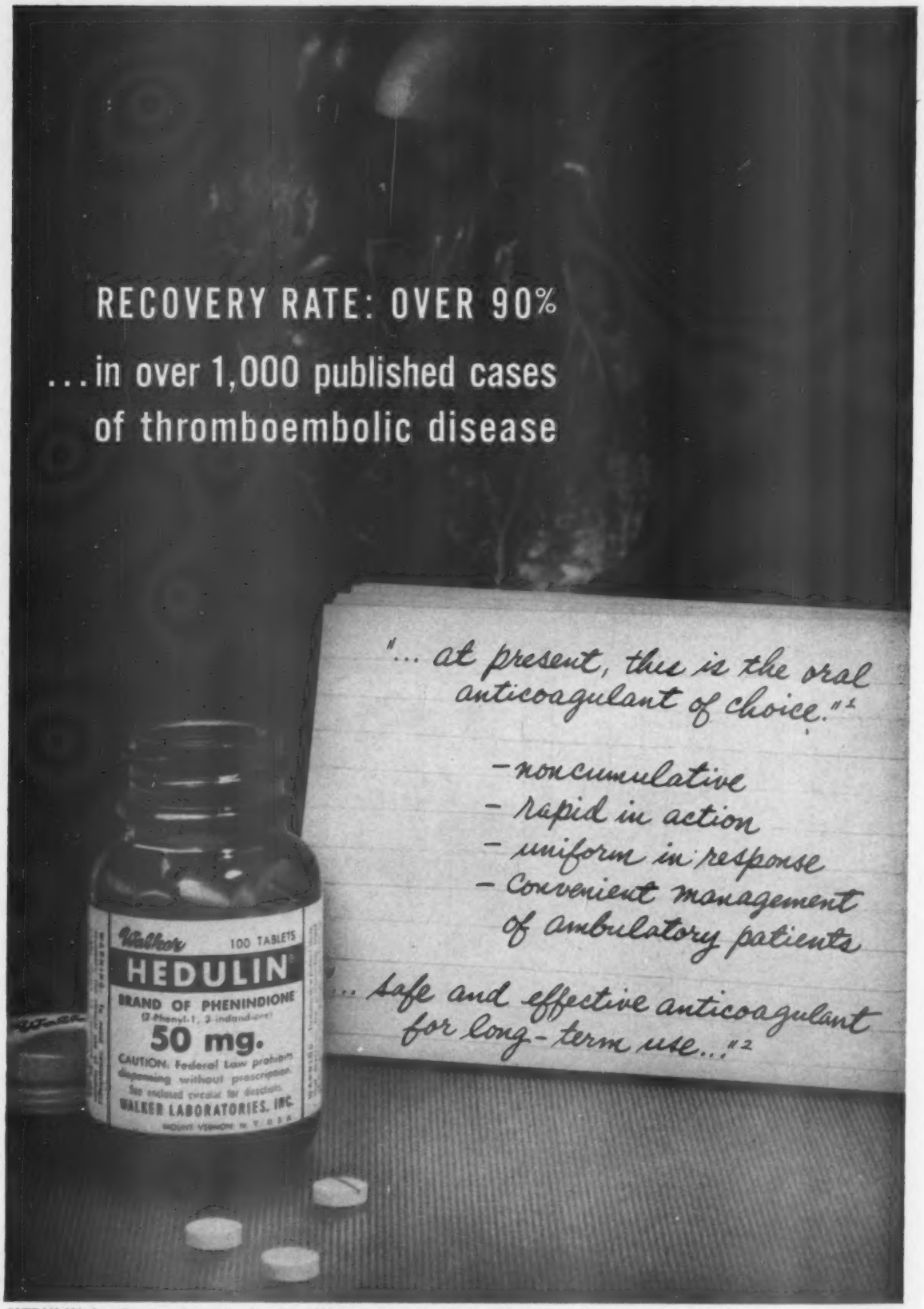
DIUPRES-250
250 mg. DIURIL (chlorothiazide),
0.125 mg. reserpine per tablet.
One tablet one to four times a day.

DIUPRES-500
500 mg. DIURIL (chlorothiazide),
0.125 mg. reserpine per tablet.
One tablet one to three times a day.

For additional information, write Professional Services, Merck Sharp & Dohme, West Point, Pa.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., WEST POINT, PA.

DIUPRES and DIURIL are trademarks of Merck & Co., Inc.



HEDULIN is the trademark for the Walker brand of phenindione. 50 mg. scored tablets for therapeutic use; 20 mg. scored tablets for prophylactic use. Bottles of 100 and 1,000. For more detailed information and a clinical trial supply of Hedulin, write to Walker Laboratories, Inc., Mount Vernon, N. Y.

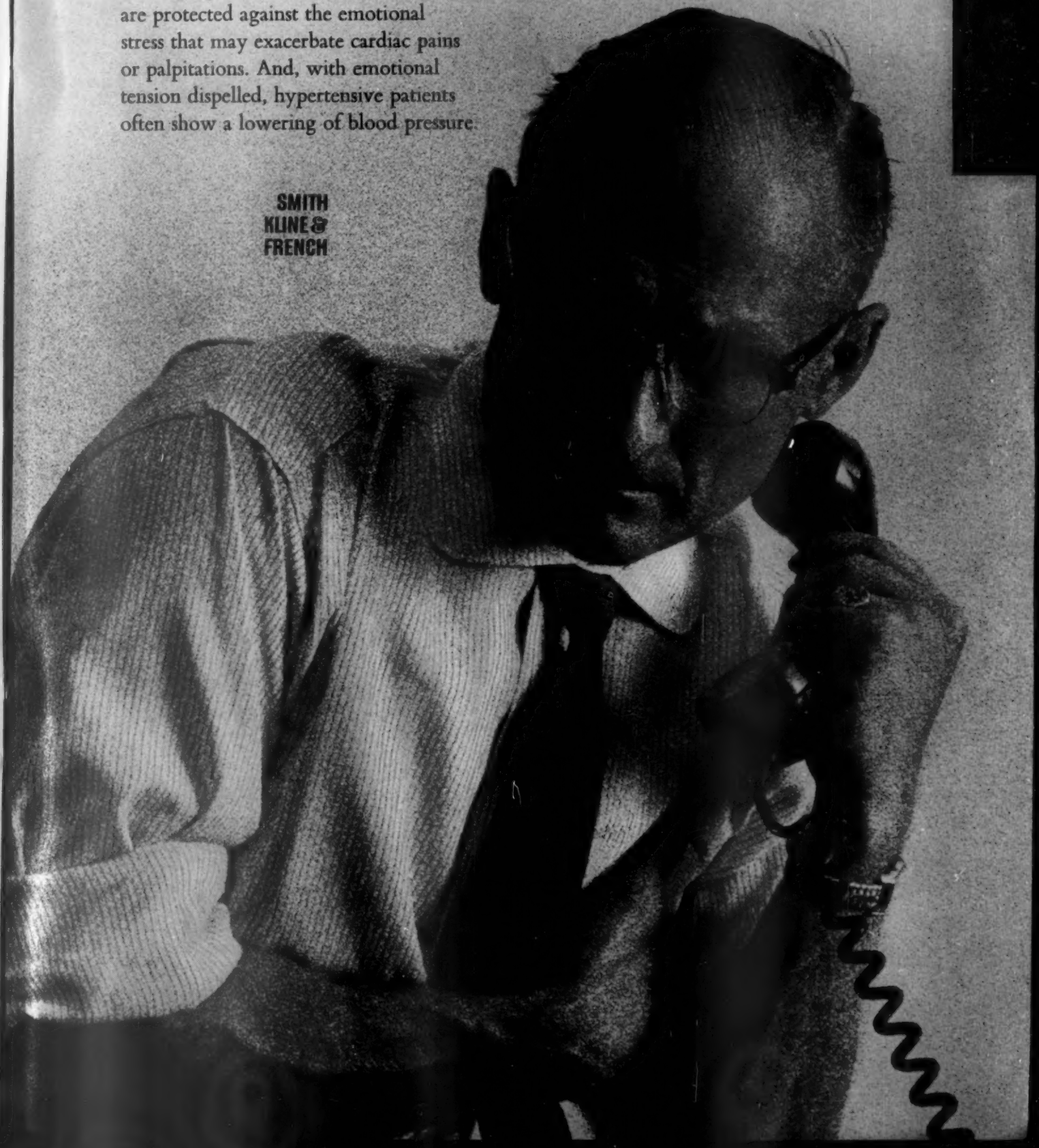
1. Breneman, G. M., and Priest, E. McC.: Am. Heart J. 50:129 (July) 1955. **2.** Tandowsky, R. M.: Am. J. Cardiol. 3:551 (April) 1959.

in cardiac patients · Compazine®

brand of prochlorperazine

reduces the impact of emotional stress—
relieves fear and apprehension.
On 'Compazine', many "heart worriers"
are protected against the emotional
stress that may exacerbate cardiac pains
or palpitations. And, with emotional
tension dispelled, hypertensive patients
often show a lowering of blood pressure.

SMITH
KLINE &
FRENCH



Advertisers' Product Index

July, 1960

*** Complete description of starred drugs will be found in MODERN DRUGS and THE MODERN DRUG ENCYCLOPEDIA**

ADVERTISING REPRESENTATIVES

New York
P. D. Brewer, H. S. Schultz, A. K. Detwiller
MUrray Hill 3-2980

AUDITED PAID CIRCULATION ABC

Chicago
R. H. Andrew, C. P. Haffner
WAbash 2-7738

safe and practical treatment of the postcoronary patient

A basic characteristic of the postcoronary patient, whether or not cholesterol levels are elevated, is his inability to clear fat from his blood stream as rapidly as the normal subject.[1-3] *Figure #1* graphically illustrates this difference in fat-clearing time by comparing atherosclerotic and normal subjects after a fat meal.[3]

"Slow clearers" gradually accumulate an excess of fat in the blood stream over a period of years as each meal adds an additional burden to an already fat-laden serum. As shown in *figure #2,* the blood literally becomes saturated with large fat particles, presenting a dual hazard to the atherosclerotic patient: the long-term danger of deposition of these fats on the vessel walls,[4] and the more immediate risk of high blood fat levels after a particularly heavy meal possibly precipitating acute coronary embarrassment.[5]

In *figure #3,* the test tube at the left contains lipemic serum, while the one at the right contains clear, or normal serum. If serum examined after a 12-hour fasting period presents a milky appearance, this is a strong indication that the patient clears fat slowly and is a candidate for antilipemic therapy in an effort to check a potentially serious situation.

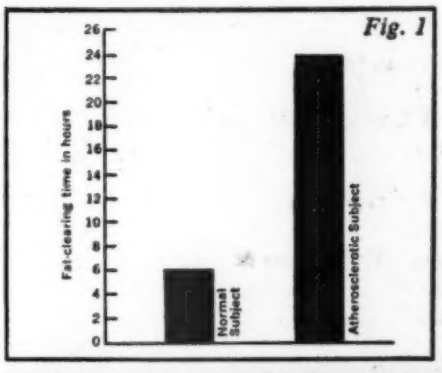
'Clarin', which is heparin in the form of a *sublingual tablet,* has been demonstrated to clear lipemic serum.[2,6,7] Furthermore, a two-year study using matched controls resulted in a statistically significant reduction of recurrent myocardial infarction in 130 patients treated with 'Clarin'.[8]

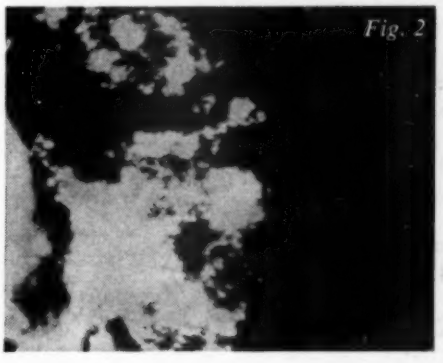
'Clarin' therapy is simple and safe, requiring no clotting-time or prothrombin determinations. Complete literature is available to physicians upon request.

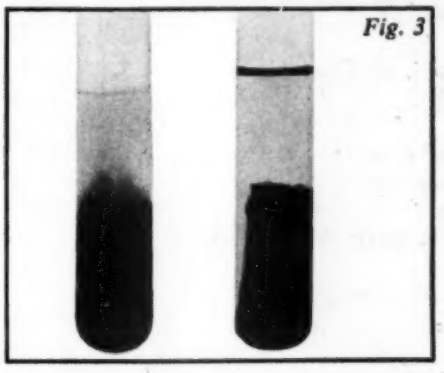
References: 1. Anfinsen, C. B.: Symposium on Atherosclerosis, National Academy of Sciences, National Research Council Publication 338, 1955, p. 218. 2. Berkowitz, D.; Likoff, W., and Spitzer, J. J.: Clin. Res. *7*:225 (Apr.) 1959. 3. Stutman, L. J., and George, M.: Clin. Res. *7*:225 (Apr.) 1959. 4. Wilkinson, C. F., Jr.: Annals of Int. Med. *45*:674 (Oct.) 1956. 5. Kuo, P. T., and Joyner, C. R., Jr.: J.A.M.A. *163*:727 (March 2) 1957. 6. Fuller, H. L.: Angiology 9:311 (Oct.) 1958. 7. Shaftel, H. E., and Selman, D.: Angiology *10*:131 (June) 1959. 8. Fuller, H. L.: Circulation *20*:699 (Oct.) 1959.

Clarin*

(sublingual heparin potassium, Leeming)







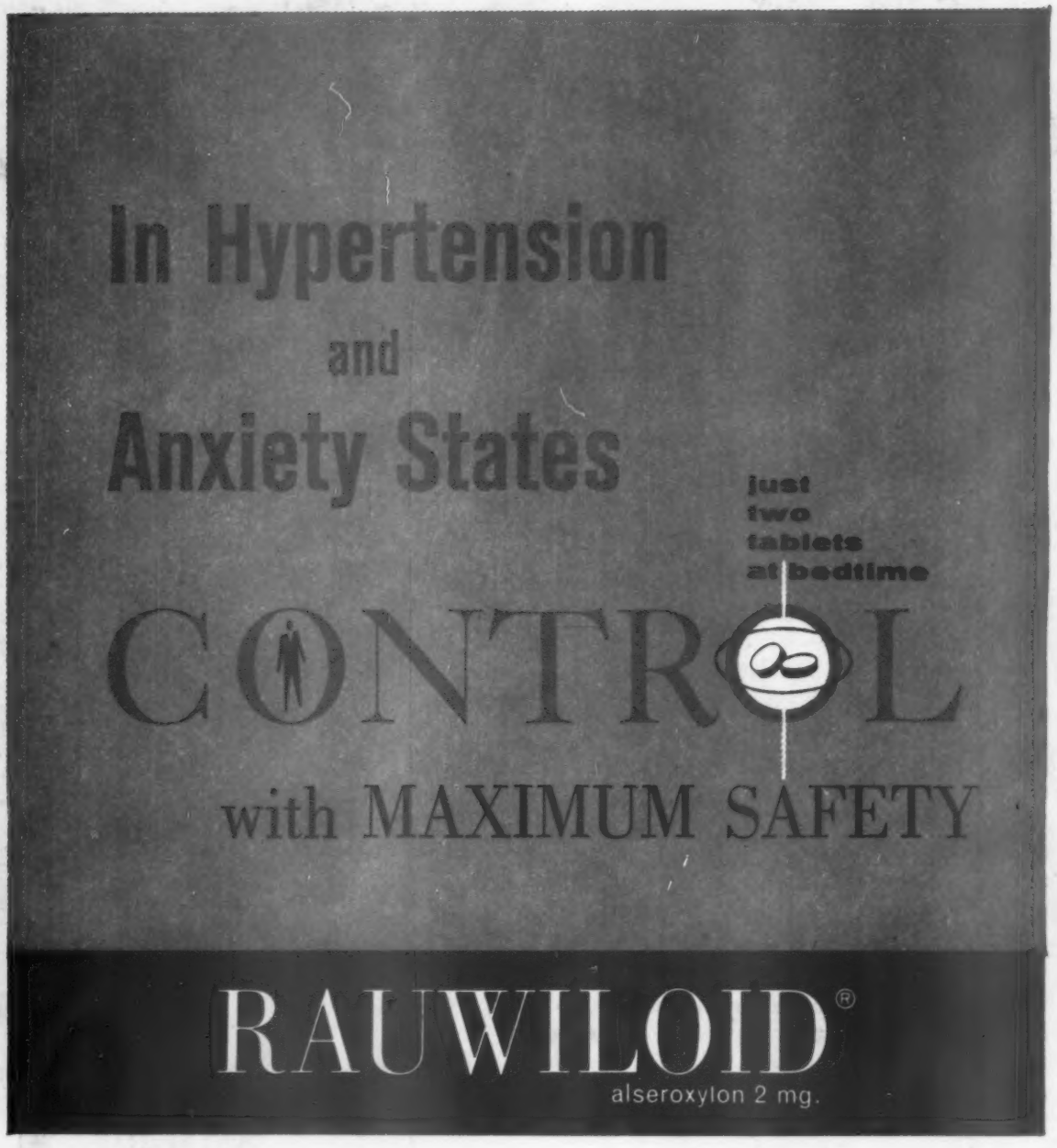
Indication: For the management of hyperlipemia associated with atherosclerosis, especially in the postcoronary patient.

Dosage: After each meal, hold one tablet under the tongue until dissolved.

Supplied: 'Clarin' is supplied in bottles of 50 pink, sublingual tablets, each containing 1500 I.U. of heparin potassium.

*Registered trade mark. Patent applied for.

Thos. Leeming & Co., Inc.
New York 17, N. Y.



In Hypertension
Simplicity of control based on negligible incidence of serious side actions, simplicity of dosage, and applicability to a wide range of patients.

In Anxiety States
Rauwiloid is outstanding for its calming, nonsoporific sedation in anxiety states...with or without hypertension.

Compatible with other antihypertensive medications. Potentiates therapeutic action of more potent agents and permits their use in reduced and better tolerated dosage.

When more potent hypotensive action is needed, prescribe one of these convenient single-tablet combinations

Rauwiloid® + Veriloid®
alseroxylon 1 mg. and alkavervir 3 mg.

or

Rauwiloid® + Hexamethonium
alseroxylon 1 mg. and hexamethonium chloride dihydrate 250 mg.

Patients with severe hypertension often can be maintained on Rauwiloid alone after desired blood pressure levels are reached with combination medication.

Riker Northridge, California